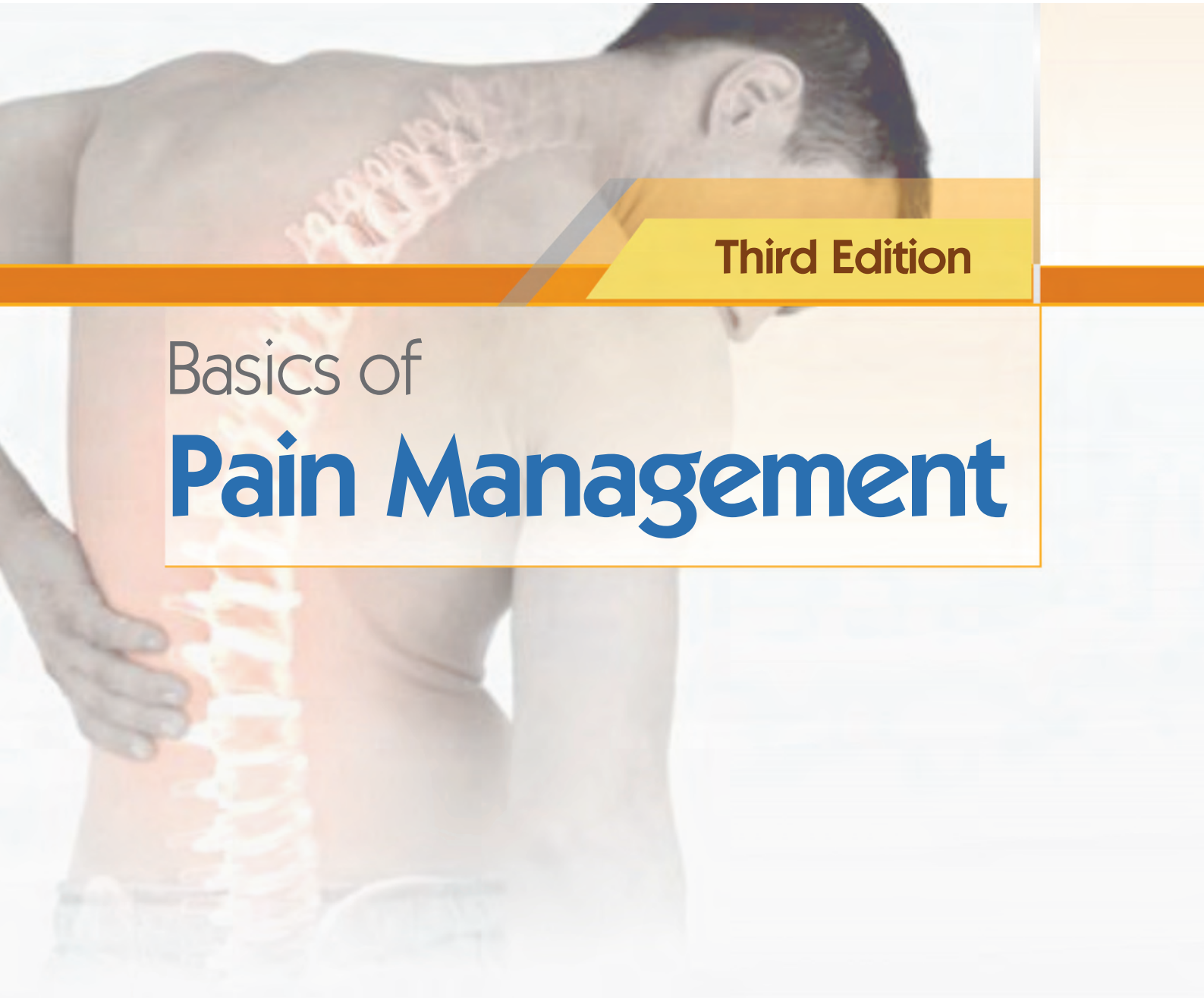

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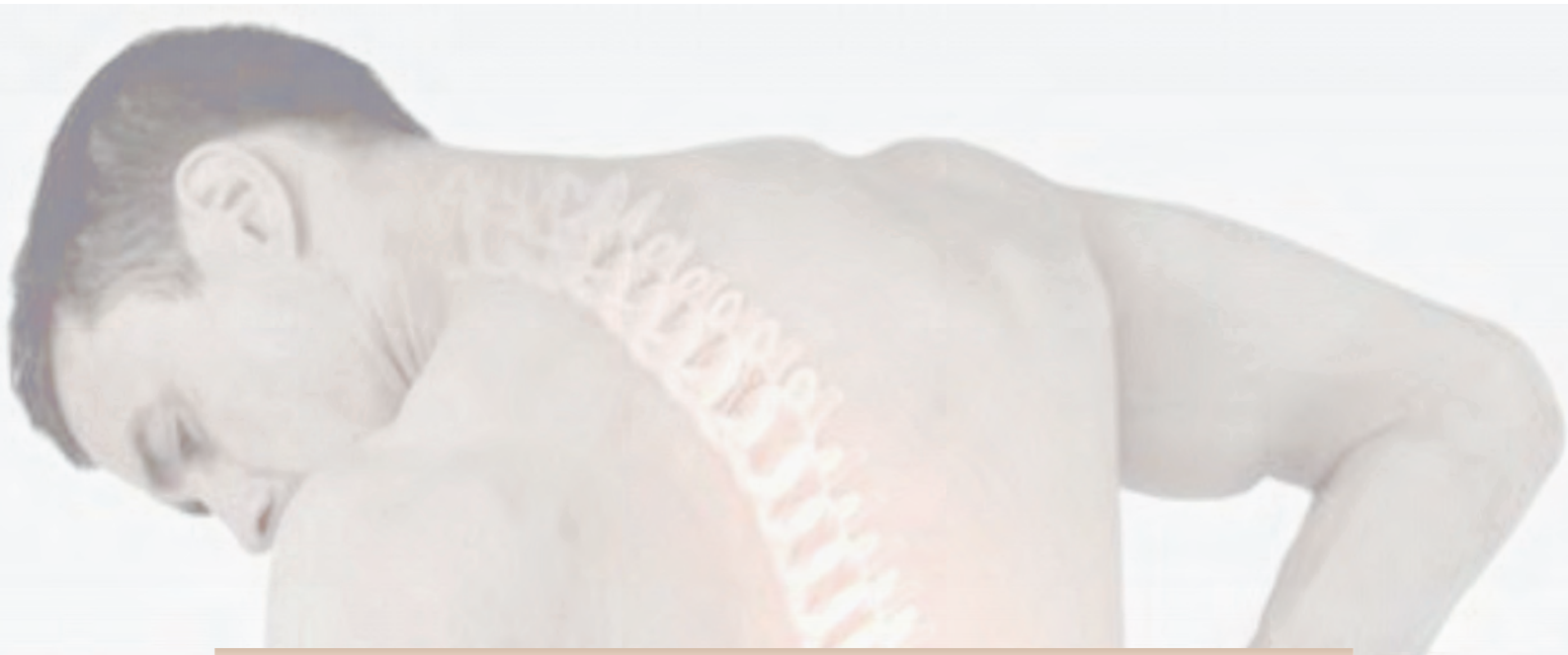

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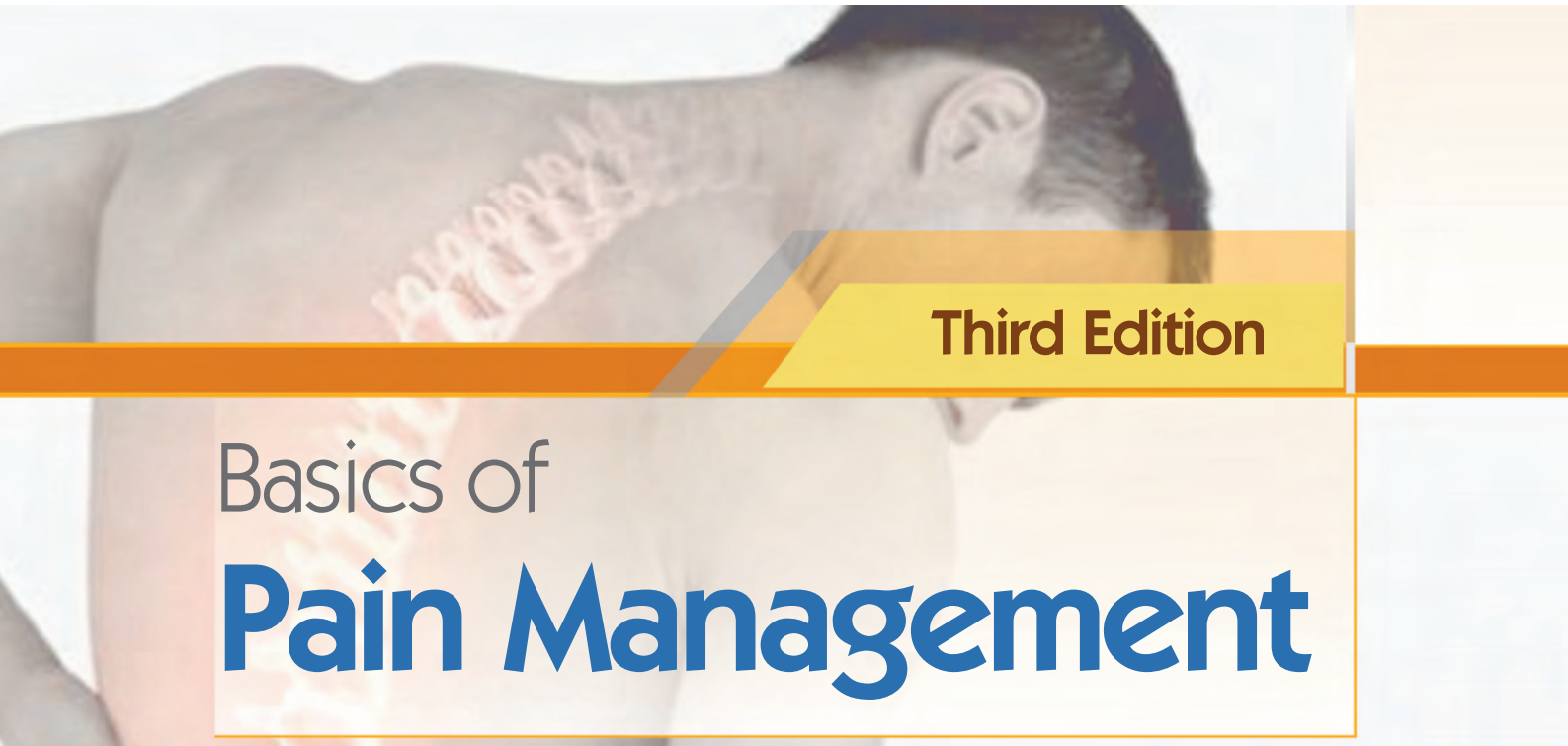

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to

My mother who has shown me the light of this earth,
My wife who has always loved me & inspired me,
My children who filled my life with happiness,
My students who helped me to compile this and other books,
My patients who taught me pain management.

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Gautam Das

Preface to the Third Edition

Author Pl. Provide Preface to the third Editoin

Preface to the First Edition

Pain is accepted as a fifth vital sign in many countries like the USA after pulse, respiration, temperature and blood pressure. It plays an important role in making us aware that something wrong is going on in our body and we need to take care of it. The basic knowledge about the pathways of pain, modulation of pain and the pathophysiology of chronic and persistent pain is very important in understanding different kind of pain in a better way. But unfortunately, in our undergraduate and postgraduate curriculums, not much emphasis has been made on this important aspect.

Various studies have shown that chronic pain in the general population is more prevalent than diabetes and hypertension. If we are not treating pain properly, it leads to depression, anxiety, mood disorder, suicidal tendencies and flaring of diabetes, hypertension, etc. Thus, it affects the quality of life and complicates our personal as well as social life.

That is why we should create awareness not only among the general population but also among physicians of all specialties in order to help the sufferers and give them a pain-free quality life.

This book is written with the intention of creating awareness about the basic knowledge of pain management not only among the pain physicians but also among the physicians of each and every other specialty.

We have started with the anatomy of pain pathways and gradually covered various painful conditions. We have not gone into the details of pathology or management of all painful conditions; rather, we have focussed on the basic concepts. We have tried to compile things in a very short and crispy manner with illustrations and diagrams so that whosoever is reading this book can go through the chapters very quickly and grasp the subject as much as possible in a short span of time.

We hope we have done justice to our work and we would be more than happy if anyone who is going through this book is at least making one individual pain-free; and giving him the quality life which he deserves.

Gautam Das

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I

General Consideration

Kanchan Sharma (Section Editor)

1. Pain Pathways
2. Types of Pain
3. Pharmacotherapy in Pain Management
4. Psychological Aspects of Chronic Pain
5. Myths in Pain Management

CHAPTER

1

Pain Pathways

Kanchan Sharma and Gautam Das

Pain is produced by the noxious stimuli perceived by specific sensory receptors called nociceptors which are there at the free nerve endings of primary afferent terminals of Aδ and C fibres. An action potential is generated at this nociceptor (transduction) which are then further carried by the Aδ and C fibres towards the higher centre (transmission) and make us feel pain (perception).

There are two important aspects which are unique to pain signal. First, whenever sensory cortex is stimulated, limbic system which controls our emotions are stimulated simultaneously. Thus emotions are the integral components of pain. Second, pain is an unique sensory signal as it is maximally changed on its way towards the higher cortical centres (modulation). The action potential generated in the periphery and the action potential that reaches the somatosensory cortex are not the same. The action potentials are either decreased (mostly in healthy individuals) or increased (anxious and chronic pain patients). Thus, the action potential that is generated at the periphery and the amount of pain that we feel do not match.

Pain: Transduction, Transmission, Modulation and Perception.

There are sequences of events which are involved in the neural processing of noxious stimuli which leads to the perception of pain (Fig. 1.1). These are:

1. ***Transduction:*** It is a process of conversion of a noxious stimuli by the nociceptors into electrical signals or action potentials. Various mechanical, thermal or chemical stimuli are responsible for the generation of these action potentials.
2. ***Transmission:*** It is a process by which the action potential generated at the nociceptor is propagated along the axon of the primary afferent neuron.

Types of afferent fibres that carries pain:

Aδ fibres are lightly myelinated with the conduction velocity of 5–15 m/sec which is faster than C fibres. They transmit rapid and sharp pain which is well localised.

C fibres are unmyelinated with the slowest conduction velocity of <2 m/sec. They carry slow, diffuse and dull pain.

The primary afferent neurons have their cell body located in the dorsal root ganglion and their central processes enter the dorsal horn in the lateral division of the dorsal root. The first order neurons synapse with the second order neurons whose axon crosses the midline and the fibres ascend in the contralateral spinothalamic tract. They synapse with the third order neurons in the thalamus and their axons project into the somatosensory cortex.

Some of the fibres project into the contralateral periaqueductal grey matter (same side of tissue damage). From periaqueductal grey matter descending

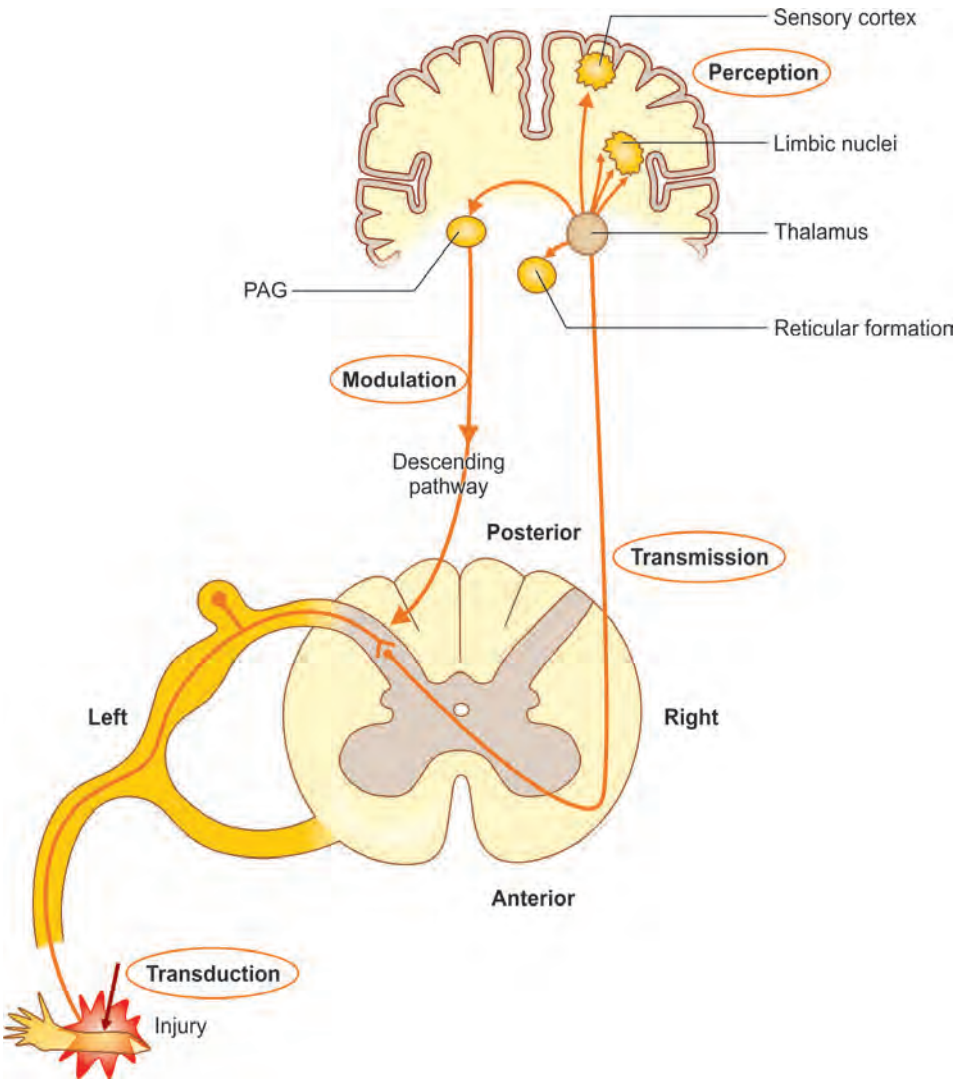


Fig. 1.1: Afferent pain pathway

inhibitory fibres (bulbospinal tract) start and some of the fibres project into different limbic nuclei.

3. ***Perception:*** The somatosensory cortex is associated with sensory and discriminative aspects of nociception, while the deeper limbic structures are associated with the affective motivation (emotional) component of the pain.
4. ***Modulation:*** It is a neural process that acts specifically to reduce the activity in the pain transmission system and reduce the perception of pain in healthy individuals. Some of the modulation systems are described below, among all of them descending inhibitory pathway plays a very important role in modulation of pain signals.

   a. Endogenous pain modulation system: Endogenous opioids like endorphins, enkephalins and dynorphins act on the opioid receptors present in the dorsal horn and results in presynaptic inhibition.

b. ***Segmental inhibition:*** Local inhibition in the dorsal horn is mediated by the release of inhibitory neurotransmitters like glycine and GABA.
c. ***Gate control theory of pain:*** It states that activating the larger diameter Aβ fibres leads to inhibition of pain signals transmitted via smaller diameter Aδ and C fibres. An inhibitory interneuron acts as a physiological gate which is closed by stimulation of Aβ fibres. It is a historical event when Melzack and Wall proposed gate control theory in 1965. Transcutaneous electrical nerve stimulation (TENS), spinal cord stimulation, peripheral nerve stimulation was established based on this principle.
d. ***Descending inhibitory pathways:*** Periaqueductal grey (PAG) and the rostral ventromedial medulla in the midbrain send descending fibres which project into the dorsal horn of the same side of tissue damage. These inhibitory neurons are activated by serotonin (5HT) and norepinephrine (NE). They send an inhibitory signal in the dorsal horn and reduce the intensity of the signal which is transmitted from first order neuron to the second order neuron. Antidepressant medications activate this system and increase the level of 5HT and NE and help in reducing the intensity of pain.

Autonomic Nervous System

The autonomic nervous system (ANS) plays an important role in different kinds of pain. For example, pain signals from thoracic or abdominal viscera and intervertebral disc or vertebral body are carried by afferent sympathetic fibres. Efferent sympathetic fibres also involved in some kinds of pain.

ANS can be defined as the neurological substrate that acts to maintain homeostasis in the body. It consists of two main divisions—parasympathetic and sympathetic nervous system. They are functionally and anatomically distinct.

Sympathetic outflow originates in the thoracolumbar region of the spinal cord and exits through spinal nerve T1–L2.

Parasympathetic nervous system, also called cranial-sacral, exits through cranial nerve 3rd (oculomotor), 7th (facial), 9th (glossopharyngeal), 10th (vagus) and S2–S3 sacral nerves.

Sympathetic Nervous System: Different configuration of the preganglionic and postganglionic fibres (Fig. 1.2)

Travel with spinal nerve

Efferent sympathetic outflow originates in the lateral horn of the spinal cord from segments T1–L2.The preganglionic neurons exit the spinal cord via the ventral horn along with the somatic motor fibres, then through ventral root and reaches up to the mixed spinal nerve. These fibres then join the sympathetic chain situated at the anterolateral border the spine via the white ramus communicants. Sympathetic chain or trunk contains sympathetic ganglion or paravertebral ganglion and extends from the base of the skull to the coccyx.

In sympathetic ganglia the preganglionic neurons synapse with the postganglionic neurons and leave through the grey ramus communicants to join the spinal nerve and follow it to supply the target effector organs.

Preganglionic fibres do not necessarily end at the same level, some fibres ascend up and end at different cervical levels and similarly some fibres descend down and end at different lumbar and sacral levels. Thus, every spinal nerve roots get sympathetic fibres via grey rami communicants. Therefore, we can say that grey rami communicants are there in all spinal nerve roots; however, white rami communicants are there only between T1 and L2.

These sympathetic fibres spreads and reach periphery via blood vessels or somatic nerves. They are of different types, vasomotor, pilomotor or sudomotor. Vasomotor fibres release catecholamines and regulate blood pressure; sudomotor and pilomotor fibres

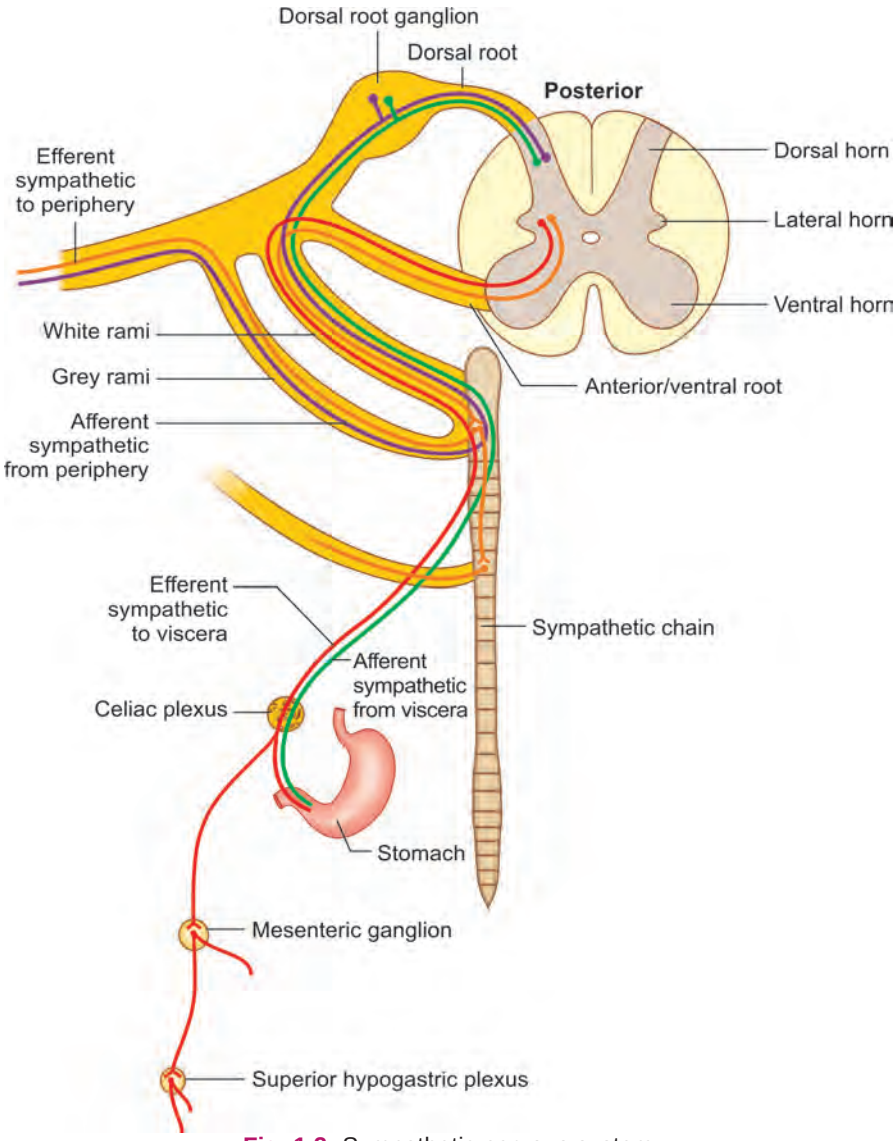


Fig. 1.2: Sympathetic nervous system

release acetylcholine and control sweating and erection of hail follicle respectively.

Visceral efferent sympathetic nerves

Preganglionic fibres join the sympathetic chain via white rami communicants in the same way as efferent sympathetic nerves that reach the periphery via somatic nerves. These preganglionic efferent sympathetic fibres neither end in sympathetic chain nor do they join grey rami communicants.

These fibres extend up to the ganglion lying close to the visceral organs (celiac ganglion). Some of the fibres end there, rests extend to the other ganglions (mesenteric, superior hypogastric, etc.). Postganglionic fibres arise from this ganglion and supply the visceral organs.

Afferent sympathetic fibres

The afferent fibres travel along with the somatic nerves and blood vessel and enter the sympathetic chain through the grey rami communicants and leave the sympathetic chain via white rami communicants and join the mixed spinal nerve. Then through the dorsal root along with the somatic sensory fibres enter the dorsal horn and end there. The afferent sympathetic system has one nerve and their cell body is situated in the dorsal root ganglion. Second order neuron are spinothalamic tract which is same for both somatic and sympathetic system.

Visceral afferent sympathetic nerves

Visceral painful stimulus is carried by the afferent sympathetic fibres in a direction opposite to that of efferent fibres. Pain signals travel via these fibres, then passes through the celiac ganglion without relaying there. These fibres via splanchnic nerves join the sympathetic chain and finally mixed spinal nerve by white rami communicants. Then through the dorsal root enters the dorsal horn.

Sympathetic Nervous System Distribution and Functions

Somatic

It supplies body wall and the skin. Each spinal nerve has got a contribution from grey ramus and supplies one spinal segmental area along with sympathetic fibres and provides three functions to the skin—vasomotor (vasoconstriction of the arterioles), pilomotor (erector pilli muscle) and sudomotor (sweat glands).

Visceral

It supplies the internal organs of head and neck, abdomen and pelvis.

Head and Neck

Postganglionic fibres arise from the sympathetic ganglion and travel along the segmental nerve and the blood vessel and supply the skin, eye.

Thorax

Postganglionic fibres from the cardiopulmonary and oesophageal plexuses supply the heart, lung and oesophagus.

Abdomen and Pelvis

Preganglionic fibres project into the ganglion:
Unlike head/neck and thoracic viscera, here preganglionic fibres from white rami after joining sympathetic trunk projects via splanchnic nerves into abdomen and forms several visceral ganglions like: Celiac, superior mesenteric, inferior mesenteric, superior hypogastric and inferior hypogastric ganglions located in front of the vertebra along the branches the aorta.

Splanchnic

Greater T5–T9: Celiac ganglion—supplies foregut. Lesser T10–T11: Superior mesenteric—supplies midgut. Least T12: Aortic renal—supplies hindgut

Somatic Sympathetic Coupling and Mechanisms of Sympathetically Mediated Pain

Somatic and sympathetic nerves are well insulated with no cross talks in between them. But with pathological conditions it may change and there is a connection between somatic and sympathetic signals.

It occurs at three sites:

1. DRG (dorsal root ganglion): Cross talk is possible here.
2. Peripheral nerve injury/Neurolysis may be followed by regeneration and sprouting which results in the exchange of signals between the somatic and sympathetic fibres. It is mostly the afferent sympathetic fibres which are mainly involved.
3. Sympathetic efferent fibres: Sympathetic efferent fibres release catecholamines, which instead of acting on sympathetic receptors may stimulate the nociceptors, which normally are stimulated by

mechanical, chemical and thermal stimuli. These nociceptors then generate action potentials which are carried by somatic nerves. The classical example is CRPS.

Sympathetic Blockade and its Significance in Pain Management

Sympathetic blockade results in the interruption of transmission by both efferent and afferent fibres. It does not result in sensory and motor loss as seen in somatic blockade.

Examples of sympathetic blockade at various levels:

1. Stellate ganglion and lumbar sympathetic blockade for CRPS of upper and lower limbs.
2. Splanchnic and celiac plexus block for upper abdominal malignancy and chronic benign pain.
3. Superior hypogastric plexus block: Cancer and non-cancer chronic pelvic pain.

BIBLIOGRAPHY

1. Beaulieu P, Rice A. Applied physiology of nociception. In: Rowbotham DJ, Macintyre PE, (Eds) Clinical Pain Management: Acute Pain. London: Arnold,2003:4-16.
2. Dostrovshy J, Craig. Ascending projection systems. In: McMahon SB, Koltzenburg M, (Eds). Wall and Melzack's Textbook of Pain. 5th edn. Elsevier Churchill Livingstone; 2006. p. 187–203.
3. Gold MS, Gebhart GF. Peripheral Pain Mechanisms and Nociceptor Sensitization In: *Fishman SM*, *Ballantyne JC*, *Rathmell JP*, (Eds). *Bonica's management of pain*. *4th edn*. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 24–34.
4. Griffin RS, Fink E, Brenner JG. Functional Neuroanatomy of the Nociceptive System In: *Fishman SM*, *Ballantyne JC*, *Rathmell JP*, editors. *Bonica's management of pain*. *4th edition*. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 98–119.
5. Jurgen Lorenz, Michael Hauck. Supraspinal Mechanisms of Pain and Nociception In: *Fishman SM*, *Ballantyne JC*, *Rathmell JP*, (Eds) *Bonica's management of pain*. *4th edn*. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 61–73.
6. Melzack's R, Wall PD. Pain mechanism: A new theory. Science 1965 Nov 19;150(3699): 971–9.
7. Meyer RA, Ringkamp M, Campbell JN, Raja SN. Peripheral mechanisms of cutaneous nociception. In: McMahon SB, Koltzenburg M, (Eds). Wall and Melzack's Textbook of Pain. 5th edn. Elsevier Churchill Livingston; 2006. p. 3–34.
8. Ness T, Randich A. Substrates of Spinal Cord Nociceptive Processing In: *Fishman SM*, *Ballantyne JC*, *Rathmell JP*, (Eds). *Bonica's management of pain*. *4th edn*. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 35–47.
9. Randich A, Ness T. Modulation of Spinal Nociceptive Processing In: *Fishman SM*, *Ballantyne JC*, *Rathmell JP*, (Eds). *Bonica's management of pain*. *4th edn*. Baltimore (MD): Lippincott, Williams & Wilkins; 2010. p. 48–60.
10. Rexed B. The cytoarchitectonic organisation of spinal cord in the cat. J Comp Neurol 1952 Jun;96(3):414–95.

CHAPTER

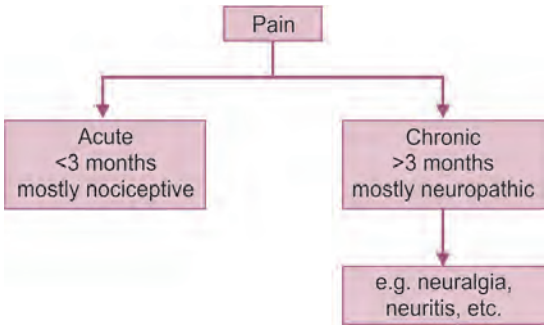
2

Types of Pain

Kanchan Sharma and Gautam Das

Definition of pain: International Association for the Study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] According to IASP even if the patient is experiencing pain in the absence of tissue damage, or any likely pathophysiological cause, it should be accepted as pain.

Different Types of Pain



Classification Based on Time: Acute Pain and Chronic Pain

Acute pain: Pain lasts for less than 3 months or which is directly related to tissue damage. Example: postoperative pain, pain because of a cut on the finger.

Chronic pain: IASP defines it to be a pain persisting for more than 3 months.[1] However, its being defined as a pain of more than 6 months' duration also.

Classification Based on Mechanism: Nociceptive Pain and Neuropathic Pain

Nociceptive pain: Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.

Neuropathic pain: Pain caused by a lesion or disease of the somatosensory nervous system (Table 2.1).

Neuralgic pain or neuritis pain are different variety of neuropathic pain.

Neuralgia: Pain in the distribution of a nerve or nerves.

Table 2.1: Difference between nociceptive and neuropathic pain

Nociceptive pain	*Neuropathic pain*
Because of non-neural tissue damage	Because of neural tissue damage
Physiological pain	Pathological pain
Simple relationship between pain and tissue damage	Dissociated relationship between pain and tissue damage
Easier to diagnose and treat	Difficult to diagnose and treat
Inflammatory pain, visceral pain are different varieties	Neuralgia, neuritis are different varieties
Paracetamol, opioids and NSAIDs are effective to reduce pain	Adjuvants or co-analgesics like anticonvulsants, antidepressants, etc. are effective to reduce pain.

Neuritis: Inflammation of a nerve or nerves. This term should not be used unless inflammation is thought to be present.

Nociplastic pain: This is a type of pain which is due to dysfunction of nerves, but there is no demonstrable damage of nerves or other tissues. This is a type of pain newly defined by IASP as follows:

"Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain."

Pathophysiology of Neuropathic Pain

Sensitization is a phenomenon of inappropriate or disproportionate response to normal stimulus which is the basis of neuropathic pain. IASP defines sensitization as "increased responsiveness of nociceptive neurons to their normal input, and/or recruitment of a response to normally subthreshold inputs."[1] "Sensitization is a key feature of neuropathic pain."

These are of two types.

Peripheral sensitization

Sensitization that happens due to changes at peripheral nerves is peripheral sensitization. IASP defines it as "increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields."[1]

The following factors play an important role in peripheral sensitization:

a. ***Up regulation of active nociceptors*:** Sleeping nociceptors awakens and new nociceptors are formed thus, the population of active nociceptors increases.
b. ***Sensitisation of the primary afferent terminals*:** Following tissue injury, there is peripheral release of neurotransmitters which sensitises nociceptors. Thus, there is increased response to low threshold stimuli and easy generation of action potentials at free nerve ending.
c. ***Ectopic discharges*:** There may be generation of ectopic action potentials at the axons of the primary afferent fibers, presynaptic terminals and the dorsal root ganglion. This happens mostly as a result of the increase sodium and calcium channel activity.
d. ***Phenotypic switching,*** This results in increased production of excitatory neuropeptides like substance P, CGRP, etc.
e. ***Somatic-sympathetic coupling*:** Sympathetic efferents release catecholamines (adrenaline and noradrenaline) which are supposed to act on sympathetic receptors. But here catecholamines will be binding and stimulating the sensitized nociceptors (which are normally are stimulated by mechanical, chemical and thermal stimuli) to generate action potentials. This action potential will be carried by somatic nerves to the higher centre.

Central sensitisation

Sensitization as a result of changes in central nervous system is called central sensitization. IASP defines central sensitization as "increased responsiveness of nociceptive neurons in the central nervous system to their normal or sub threshold afferent input."[1]

The following factors are components of central sensitization:

a. ***Central reorganisation:*** Following nerve injury A beta fibres form convergence in lamina II and synapse with the neurons conveying nociception resulting in mechanical allodynia. The area of pain increases along the distribution of other nerves due to activation of interneurons at the spinal level. There is loss of function of descending inhibitory pathways.
b. ***Disinhibition:*** There will be down regulation of inhibitory neurotransmitters GABA, glycine and opioids receptors in the dorsal

horn of spinal cord.

c. ***Ectopic discharges:*** Facilitation of the excitatory synapses.

d. ***Wind up phenomenon***: Repeated stimulation of C fibres results in the temporal summation of inputs from them and results in increase in the excitatory stimulus.

e. ***Activation of WDR neurons.*** Wide dynamic range (WDR) cells are recruited in the pain pathway.

Results of sensitization

a. Increase in the intensity, area and duration of pain
b. Decrease in the tolerability of pain
c. Development of psychological problems
d. Pain becomes unresponsive to conventional analgesics.

Diagnosis of neuropathic pain: Making a diagnosis based on patient's complains is the keystone in laying down the foundation of treatment plans. The correct treatment plans target the right pain generator and the pathophysiology behind it.

Features of neuropathic pain

a. Pain in the area of neurodeficit or numbness
b. Allodynia
c. Hyperalgesia
d. Character of pain: Burning, shooting, electric shock like, stabbing
e. Associated symptoms: Numbness, tingling, pruritis, feeling of pin and needles

Pain history: Detail history taking plays an important role in locating the pain generators and it avoids unnecessary investigations at the same time. Special attention needs to be given to anxious, depressed or overtly frightened, patients who over a period of time have started feeling hopeless regarding the treatment of their pain.

History is also very important in ruling out the red flags such as trauma, infection, tumour, progressive motor and sensory deficit, which needs more invasive management and treatment. Sufficient time to be given to the patients to express their problems for which they are seeking our medical care. We should listen carefully without any distraction in order to interpret the information provided by the patient.

It includes: onset, site, duration, localized/or diffuse, night pain, aggravating and relieving factors, radiation, periodicity.

Quantitative measurement of pain: Pain is a subjective feeling that is why we need to rely on patient's version. Current pain intensity and average pain intensity over a specified period of time, e.g. last 1 week or 4 weeks should be noted down. The main aim of treatment lies in reducing the intensity of pain at the same time avoiding the side effects and increasing the patient acceptance towards treatment. Numerous pain scales have been devised to measure the intensity. They not only help us in measuring the intensity, but also help us in assessing the patient's response towards treatment.

Examples of scales used for the quantitative measurement of pain:

NRS scale: Patient is asked to indicate the current intensity of his pain on a scale which has "0" at one end, which corresponds to "no pain" and "10" at the other end which corresponds to "worst pain imaginable". A score of 1–3 indicates mild pain, 4–6 indicates moderate pain and 7–9 indicates severe pain (Fig. 2.1).[2,3]

The visual analogue scale (VAS): It is similar to the numerical rating scale. There is a 10 cm horizontal line with a label of "no pain" at one end and "worst pain imaginable" at the other end. The patient is asked to mark on this line where he feels the intensity of his/her pain lies. The distance from "no pain" to this mark indicates the severity of pain numerically. Slide rule-like devices are also available that make measurement easier. The device has a line on the patient side and a numeric score

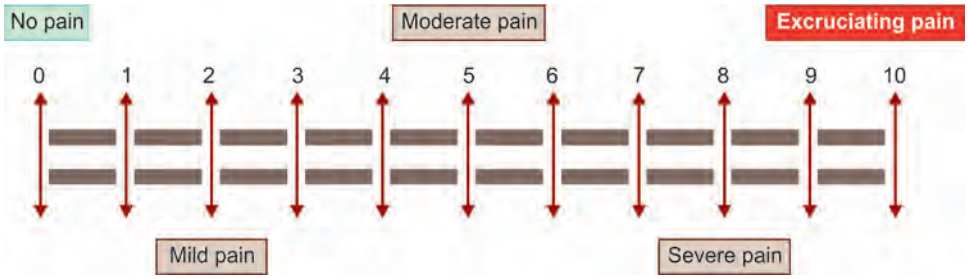


Fig. 2.1: Pain scale

on the clinician side. The VAS is a simple, efficient, valid and minimally intrusive method that correlates well with other reliable methods. The disadvantage is that it is more time-consuming than other instruments. There is some difficulty in using and understanding this scale in elderly patients.[2,5–6]

Qualitative Measurement of Pain

Pain DETECT tool: It is a self-report questionnaire which consists of seven sensory descriptors, items (burning sensation, tingling or prickling sensation, pain on touching, electric shock like, cold or heat intolerance, numbness, pain on slight pressure) and two items related to the spatial (radiation) and temporal characteristic of patient individual pain pattern.

Its sensitivity is 85% and specificity is 80% respectively. Sensory descriptors are scored on a 0 (no symptom) to 5 (strongest symptom) scale.

Radiation is scored as present "+2" or absent "0".

Temporal characteristics are scored as persistent pain with slight fluctuations "0", persistent pain with pain attacks "–1", pain attacks without pain between them "+1", and pain attacks with pain between them "+1".

We have to add up the total score. If the total score is less than 12, neuropathic component is unlikely. In between 13–18 neuropathic component can be present. If the score is greater than 18, neuropathic component is likely.[7]

Leeds assessment of neuropathic symptoms and signs (LANSS): It is a screening test to identify the pain of neuropathic origin. It is a simple tool with two components. A questionnaire which consists of 5 symptoms, addressing pain quality and triggers and second one sensory testing, which consists of 2 signs. Each item is a binary response (yes or no) to the presence of symptoms (5 items) or clinical signs (2 items). It is easy to score in clinical settings and has been tested and validated in a number of neuropathic pain conditions with a sensitivity and specificity ranging from 82 to 91% and 80 to 94% respectively.

Score <12/24 indicates that the pain is unlikely to be neuropathic in origin and Score >12/24 indicate that the pain is likely to be neuropathic in origin. The need for clinical examination and pin prick testing limits its use in clinical settings. In order to overcome this drawback, a self-report tool, S-LANSS has been developed and validated to identify patients whose pain is dominated by neuropathic mechanisms.[8–12]

Treatment Outline

It involves a multimodal approach to make the patient pain free. It includes the following:

a. Analgesics and coanalgesics: Analgesics like nonsteroidal anti-inflammatory drugs (NSAIDs), like paracetamol and opioids for nociceptive pain, coanalgesics like anti-convulsants and antidepressants for chronic pain or neuropathic pain.

b. Interventional pain management: Different kinds of pain interventions has revolutionized pain management. Pain interventions ranges from simple simple trigger point interventions to radio-frequency ablations to minimally invasive endoscopic spine interventions.

c. Psychological interventions: Chronic pain and depression when co-exist together effects functional abilities, personality, social as well as professional life.

d. Rehabilitation: Physical exercises, yoga, etc.

REFERENCES

1. Http://www.iasp-pain.org/Taxonomy#Pain
2. Das G. Clinical methods in Pain Medicine. CBS Publishers and Distributors. New Delhi: 2015.p. 2–17.
3. McCaffery, M, Beebe, A, et al. Pain: Clinical manual for nursing practice, Mosby St. Louis, MO. 1989.
4. Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomenon. Res Nurs Health. 1990 Aug; 13(4):227–36.
5. Freynhagen R, Baron R, Gockel U, Tölle TR. Curr Med Res Opin. 2006;Oct;22(10):1911–20.
6. Potter J, Higginson IJ, Scadding JW, et al. Identifying neuropathic pain in patients with head and neck cancer: Use of the Leeds Assessment of Neuropathic Symptoms and Signs Scale. J R Soc Med 2003;96:379–83.
7. Yucel A, Senocak M, Kocasoy Orhan E, et al. Results of the Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale in Turkey: A validation study. J Pain 2004;5: 427–32.
8. Khedr EM, Kotb H, Kamel NF, et al. Long-lasting analgesic effects of daily sessions of repetitive transcranial magnetic stimulation in central and peripheral neuropathic pain. J Neurol Neurosurg Psychiatry 2005;76:833–8.
9. Kaki AM, El-Yaski AZ, Youseif E. Identifying neuropathic pain among patients with chronic low back pain: Use of the Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale. Reg Anesth Pain Med 2005;30:422–8.
10. Bennett MI, Smith BH, Torrance N, et al. The S-LANSS score for identifying pain of predominantly neuropathic origin: Validation for use in clinical and postal research. J Pain 2005;6: 149–58.
11. Meyer RA, Ringkamp M, Campbell JN, Raja SN. Peripheral mechanisms of cutaneous nociception. In: McMahon SB, Koltzenburg M, (Eds). Wall and Melzack's Textbook of Pain. 5th edn. Elsevier Churchill Livingston; 2006; p. 3–34.
12. Serpell M: Oxford Handbook of Pain Management. Correct Medicine Group. London; 2008; p. 1–35

CHAPTER

3

Pharmacotherapy in Pain Management

Mousumi Datta and Gautam Das

Most common method of managing any type of pain is pharmacotherapy or use of drugs. Complexity of pain pathway[1] and variation of pathophysiology of pain make the list of drugs used in pain management a longer one.[2]

According to pathophysiology, pain can be nociceptive, neuropathic or mixed.

Nociceptive pain is caused by damage or disease of non-neural tissues and because of activation or sensitization of peripheral

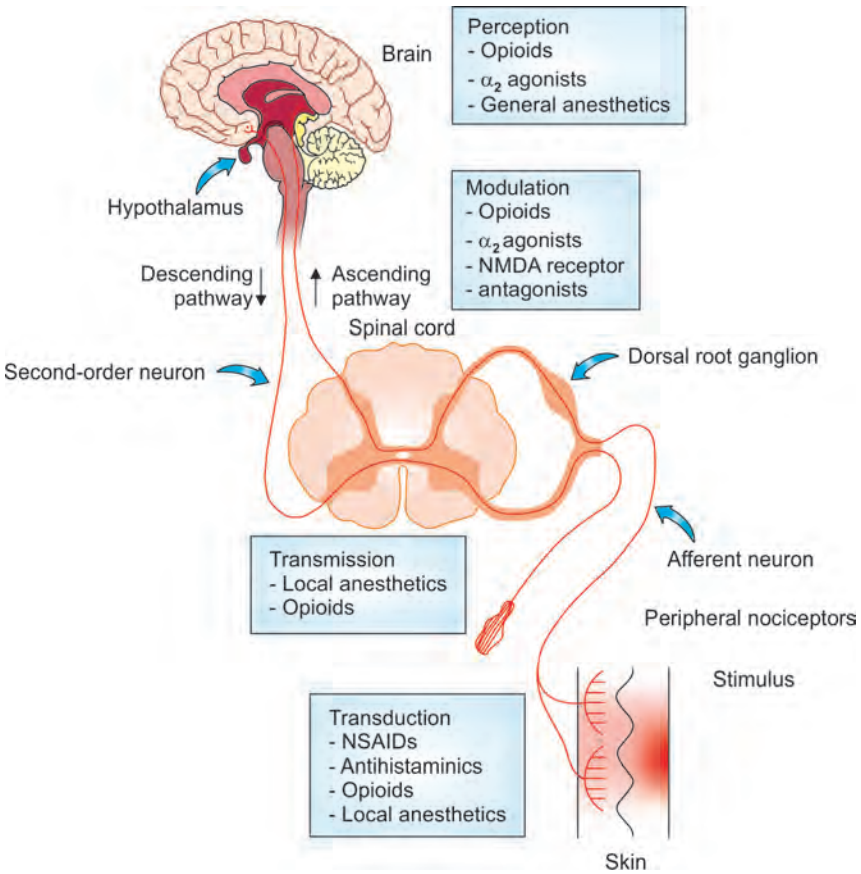


Fig.3.1: Therapeutic modulation of pain processing pathway: use of different drugs. [NMDA: N Methyl D Aspartate; NSAIDS: nonsteroidal anti-inflammatory drugs][3]

nociceptors, specialized receptors that transduce noxious stimuli. That's why nociceptive pain responds well to simple analgesics like anti-inflammatory and opioid medication. But neuropathic pain, where the pathology is due to damage or dysfunction of nervous system not directly due to tissue damage, responds better to co-analgesics like anticonvulsants and antidepressants.[4–6]

Drugs used in pain management can be categorized under two broad headings:

- Analgesics
- Co-analgesics

Analgesics are:

- Anti-inflammatory, non-selective COX-inhibitors like NSAIDs, selective COX-2 inhibitors
- Acetaminophen/paracetamol
- Opioids.

Co-analgesics or adjuvant group includes:

- Anticonvulsants
- Antidepressants
- Local anesthetics
- Steroids
- Muscle relaxants
- Botulinum toxins
- NMDA receptor antagonists
- Others like α_2 agonist, calcium channel blockers, vitamins and nutrisuppliments, etc.

Rational pharmacotherapy for pain:

- It should effectively control the pain.
- Treat the cause of the pain: Act on the pathological part of the pain pathway.
- Patient Preference: Symptom control versus side effects should be considered.

Drugs should have:

- Minimal side effects.
- Easily self-administered
- Minimal risk associated with long-term use
- Rapid onset and long-acting
- Safely combined with other therapy.

WHO Step Ladder

World Health Organization (WHO) made a very simple and effective way for dealing with drugs in pain patients. WHO in 1986 started a stepwise approach popularly known as 'WHO stepladder'.

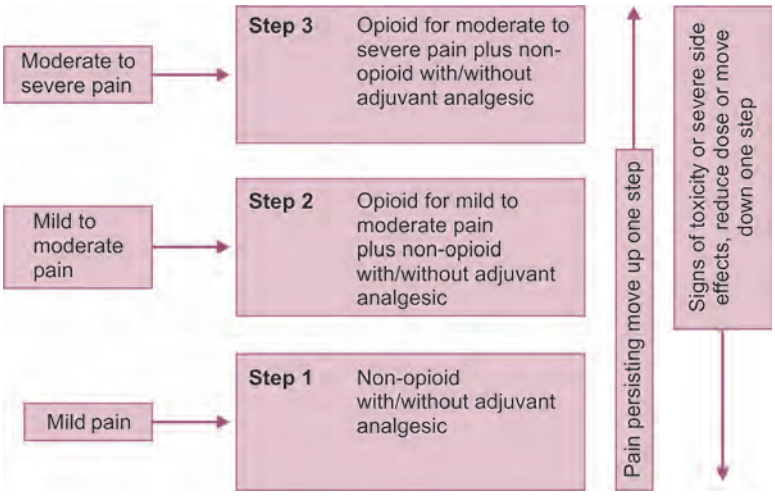

Moderate to severe pain
Step 3
Opioid for moderate to severe pain plus non-opioid with/without adjuvant analgesic
Mild to moderate pain
Step 2
Opioid for mild to moderate pain plus non-opioid with/without adjuvant analgesic
Mild pain
Step 1
Non-opioid with/without adjuvant analgesic
Pain persisting move up one step
Signs of toxicity or severe side effects, reduce dose or move down one step

Fig. 3.2: The World Health Organization (WHO) analgesic ladder. (*Adapted from* World Health Organization: cancer pain relief. Geneva, WHO, 1990)[4,12]

(*see* Chapter 28 "Pharmacotherapy in Cancer Pain").

Analgesics[1–3, 7–12]

Anti-inflammatory COX-inhibitors: NSAIDs, COX-2 inhibitors

- **Mechanism of action:** Inhibit both peripheral and central cyclooxygenase (COX), reduce prostaglandin formation.
- **There are two isoform of COX:** COX-1 (constitutive, physiologic) and COX-2 (inducible, inflammatory). Mostly COX-2 is responsible for pain and sensitization.
- COX-2 selective inhibitors have better gastrointestinal safety profile and least effect on platelet function.
- These drugs are indicated in mild to moderate pain associated with acute or chronic inflammation. Condition like rheumatoid arthritis, osteoarthritis, ankylosing spondylitis where inflammation is the main pathology or acute pain like fracture, postoperative pain where there is definitive tissue damage respond to NSAIDs well.
- NSAIDs are good analgesics but their action is limited by side effects and toxicity at higher dose.
- As COX-1 is involved in gastric protection, NSAIDs are known to have adverse effect on GI system.
- Selective COX-2 inhibitors have less GI and renal side effects. Those also do not interfere with platelet aggregation. But they are known to cause cardiovascular complications.

Paracetamol

- The mechanism of action of paracetamol is still unclear. It has some action on COX-3 isoenzyme. Thus inhibit prostaglandin synthesis. The anti-nociceptive action is partly mediated by central serotonergic mechanism. It also modulates central cannabinoid system.
- It has little anti-inflammatory and no antiplatelet activity.
- Paracetamol has less potential for GI irritation and safer for kidney but known for dose-dependent hepatotoxicity.
- It is the first line treatment for mild to moderate pain.
- Oral dose is 325–1000 mg/6–8 hours (15 mg/kg bodyweight). Maximum dose should not exceed 4 g/day.

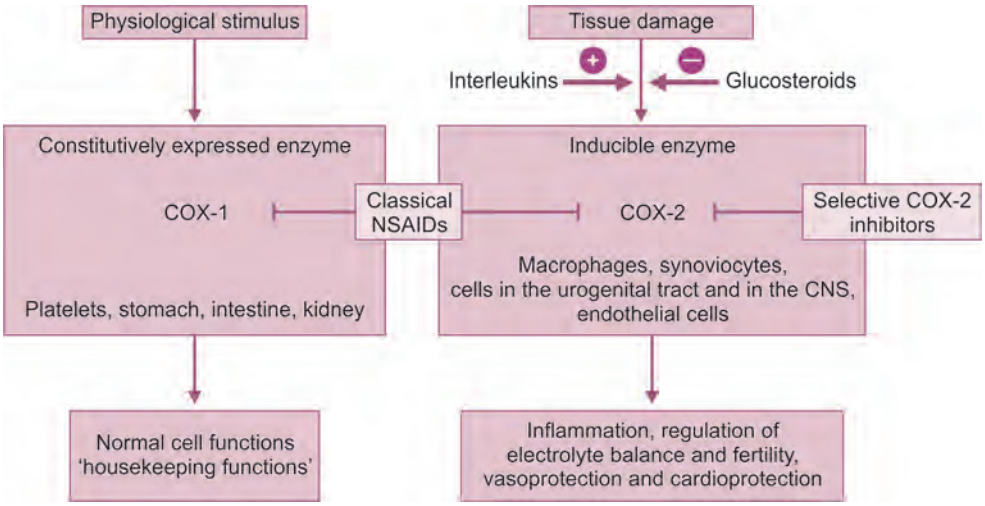


Fig. 3.3: Simplified description of the physiological and pathological roles of COX-1 and COX-2; action site of NSAIDs[1]

Table 3.1: Commonly used NSAIDs

Drug name	*Dose (mg) – oral dose range (max) in mg*	*Special points*
Ibuprofen	200–800 (1200) 8–12 hours	Interferes with platelet aggregation and clot formation, avoid use in patients with bleeding diathesis. To be used with caution in patients with asthma.
Diclofenac sodium	25–75 (200) 12 hours	Accumulates in synovial fluid, useful in OA, RA. Should be avoided in children, pregnant nursing women.
Nimesulide	100 12 hours	COX-2 preferential inhibitor lesser GI irritation.
Ketoprofen	300–600 6–8 hours	One high potency drug with fast elimination.
Naproxen	250–500 (1375) 8–12 hours	Favorable GI profile plasma half-life is 13 hours, twice a day dose is enough.
Piroxicam	20 (40) 12–24 hours	Long half-life thus to be used with caution in elderly. Takes as long as 1 week to achieve steady concentration.
Etoricoxib	60–120 (180) 24 hours	COX-2 specific inhibitors. In patients with cardiac risk should be used with caution and low dose aspirin to be added.
Mefenamic acid	500 8–12 hours	Common side effect is diarrhea. May cause severe pancytopenia.

Opioids

- Opioids can be classified according to their receptor activity, or duration of action (long-acting and short-acting) or their analgesic action and ceiling effects (weak and strong opioids).
- Opioid receptors are G-protein coupled receptors. μ is the major receptor responsible for analgesia.
- Pure agonists like morphine are preferred in moderate to severe chronic pain like cancer pain. Agonist-antagonists have ceiling effect for analgesia.
- Commonly used weak opioids are tramadol, tapentadol, codeine. Strong opioids are morphine, fentanyl, buprenorphine.
- Long-acting opioids are good to treat the baseline pain whereas short-acting opioids are useful in breakthrough pain.
- If a trial of opioids is considered then:
  - Patient should be explained the benefits and risks of opioid use.
  - WHO analgesic ladder to be followed.
  - Strong opioids like morphine should never be used as a SOS drug.
  - Side effects should be explained and measures to be taken to correct them if possible.
  - For elders 'start low and go slow'.

Table 3.2: The desirable and undesirable properties of morphine as an analgesic

Desirable	*Undesirable*
Analgesic Mood effects Sedation	Sedation Mental clouding Dizziness Mood effects Dysphoria Nausea and vomiting Respiratory depression Suppression of the cough reflex
Tolerance (to respiratory depression)	Tolerance (to analgesia) Physical dependence Substance dependence or addiction Spasmogenic Constipation

  - Instructions for follow-up and emergency should be provided.
- Oral route is preferred route of administration. Others are subcutaneous, IM, IV, transdermal, etc. transdermal patches are newer convenient method of delivery of drugs. Intrathecal pumps are also helpful for long-term opioid use.
- Tramadol: It is a unique agents with dual mechanism of analgesia. It has a weak affinity for μ-receptors and it weakly inhibits serotonin and norepinephrine reuptake. Due to dose dependent adverse effects, a gradual titration from 50 mg 2–3 times daily to a maximal dose of 200 mg twice daily is generally required.
- Nefopam: It is a non-steroidal, non-opioid, centrally acting analgesic drug. It belongs to benzoxazocine chemical class and exact mechanism of analgesic action is not nicely understood. Possible sites of action are seratonergic, dopaminergic and noradrenalie fibres where it inhibit their reuptakes and induce analgesia. Usial doses in an adult is 30 mg three times per day. It is effective in both acute and chronic pain.

Co-analgesics/Adjuvants[2–3, 5–13]

Anticonvulsants

- Anticonvulsants are commonly used adjuvant or coanalgesics in neuropathic pain.
- Both epilepsy and neuropathic pain are associated with excess neuronal activity; therefore, both may be treated with anticonvulsants to either block excitatory or promote inhibitory mechanisms.
- They are mostly either sodium or calcium channel blockers, raise the threshold for nerve depolarization. Thus suppress abnormal neural discharges.
- Drugs should be started at a low dose then gradually titrated up to therapeutic level.
- A trial period of at least 4 to 8 weeks requires to obtain pain relief.

Antidepressants

- These drugs show a direct analgesic effect at a dose much lower than that required for antidepressant action.

Table 3.3: Commonly used anticonvulsants in pain practice

Drug name	*Dose*	*Mechanism of action*	*Side effects*
Gabapentin	Starting dose 100–300 HS Usual dose 900–3600 mg in 3 divided doses Max dose 4800/day	Membrane stabilizer by binding at α2δ subunit of L-type calcium channel	Dizziness, somnolence, fatigue peripheral edema
Pregabalin			Dizziness, somnolence, fatigue peripheral edema, ataxia
Carbamazepine	Starting dose 100 mg/day Max dose 1800 mg/day	Sodium channel blocker. Inhibit pain via central and peripheral mechanism	Aplastic anemia, agranulocytosis, leukopenia, sedation, gait alteration
Oxcarbazepine	Starting dose 300 mg/day Max dose 1200–2400 mg/day	May be by modulating voltage activated calcium current	Risk of hyponatremia in first few months
Topiramate	Starting dose 50 mg/day Max dose 200 mg/day	Enhances action of GABA, inhibit AMPA type glutamate	Sedation, may predispose glaucoma and renal calculi
Lamotrigine	Starting dose 20–50 mg/day Max dose 300–500 mg/day	Prevent release of glutamate	Rash, drug should be slowly tapered off

Table 3.4: Commonly used antidepressants in pain practice

Drug name	*Oral dose in mg/duration*	*Clinical consideration*
Amitriptyline (TCA)	10–25/12–24 hours	Caution in elderly male urinary retention
Nortriptyline (TCA)	10–25/12–24 hours	Better tolerated than amitriptyline
Duloxetine algia (SNRI)	20–60/12–24 hours	DOC in diabetic peripheral neuropathy and fibromy- (FDA approved)
Milnacipran (SNRI)	50–100/12–24 hours	FDA approved drug for fibromyalgia
Venlafaxine (SNRI)	37.5–112.5/12–24 hours	SNRI better tolerated
Desipramine (TCA)	10–25/24 hours	Better tolerated TCA in elderly

Table 3.5: Side effects of TCA[5]

Side effect	*Drug class and examples*	*Comments*
Cardiovascular effects	TCAs cause postural hypotension, nortriptyline and doxepin less than imipramine, amitriptyline, desipramine, clomipramine	Most serious in elderly patients with increased risk of falling and hip fractures
	TCAs have also been shown to increase the incidence of cardiac arrhythmias in patients with existing cardiac disease	There might even be a risk of this side effect in patients without evidence of cardiovascular disease.
Sedation	Common with all TCAs; nortriptyline less common and the SSRIs and desipramine can produce insomnia	The sedating TCAs are often used at night to take advantage of their sedation. To avoid falling, care should be taken with patients who frequently get up at night.
Anticholinergic effects	Imipramine, amitriptyline and doxepin show strong effects, less so with nortriptyline, desipramine, SSRIs lack this effect	Manifested by dry mouth, constipation, and urinary retention
Weight change	TCAs cause increased appetite, SSRIs can lead to anorexia and some weight loss.	Consider drug class based on weight goals for patient.
Sexual dysfunction	TCAs and SSRIs have all been reported to have sexual side effects.	Consider dose reduction or plan sexual activity with trough levels of drug.
Psychiatric complications	Use TCAs with caution in suicidal patients; can trigger mania in bipolar patients	Seek psychiatric help for patients with complicated psychological history.
Withdrawal symptoms	Both SSRIs and TCAs	Wean all antidepressants; avoid abrupt discontinuation.
Central serotonin syndrome	Can be caused by combinations of SSRIs and TCAs	Use these combinations with caution.
Analgestic effects	Strong analgesics include imipramine, amitriptyline, nortriptyline, and desipramine. Less analgesic are SSRIs. Venlafaxine and bupropion might have some analgesic activity.	Balance dose, side effects, and analgesic activity; consider adding anticonvulsant to lower antidepressant dose when partial response to antidepressant alone

- Analgesic effect is accompanied by sedation, diminished anxiety, muscle relaxation, and restored sleep cycle.
- **Mechanism of action:** Due to blockade of presynaptic reuptake of serotonin, norepinephrine or both. They act on the descending inhibitory pain pathway.
- Depending on MOA anti-depressant drug groups are TCA (tricyclic anti-depressant), SSRI (selective serotonin reuptake inhibitors), SNRI (serotonin-norepinephrine reuptake inhibitors).
- Side effects are sedation, anticholinergic action, orthostatic hypotension, diarrhea or constipation.

Muscle Relaxants

Different muscle ralaxants are used to treat pain particularly when it is associated with muscular spasm. Some are centrally acting and some are peripheral muscle relaxants.

Table 3.6: Classification of muscle relaxants by proposed mechanism of action[13]

CNS Depressants
Antihistamine—orphenadrine Sedative—carisoprodol, chlorzoxazone, metaxalone, methocarbamol TCA-like—cyclobenzaprine
Central α_2 Agonists
Tizanidine
GABA Agonists
Baclofen, benzodiazepines

CNS: central nervous system, GABA: gamma-aminobutyric acid, TCA: tricyclic antidepressant.

Steroids

Glucocorticoids are extensively used in pain management for their anti-inflammatory and possibly analgesic actions. Route of administration can be oral, patenteral, intravenous , subcutaneous, intra-articular, epidural, or

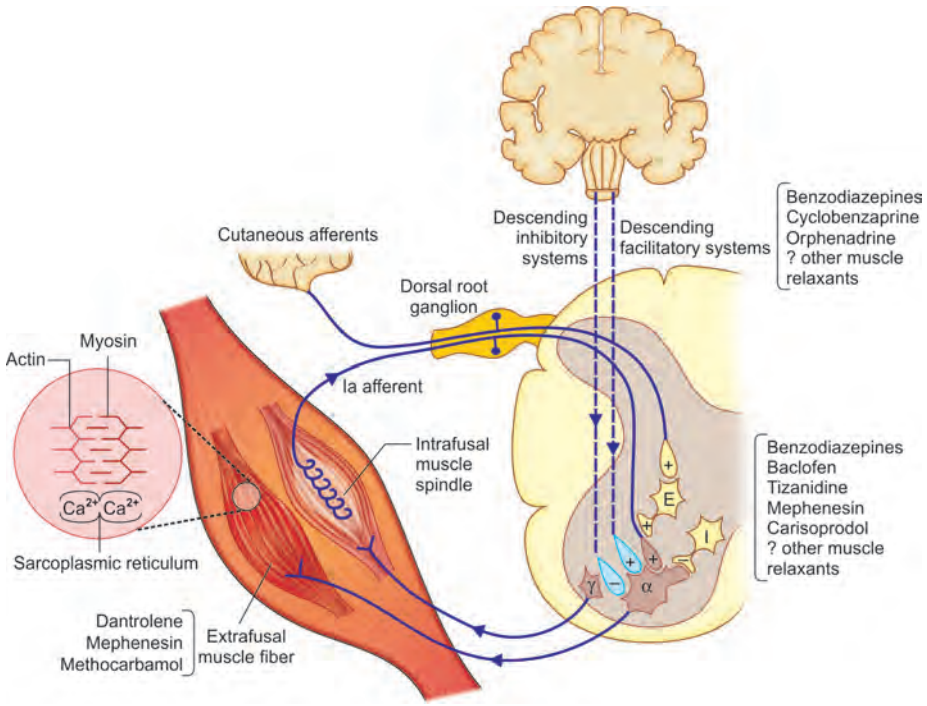


Fig. 3.4: Neural regulation of muscle tone; possible site of action of skeletal muscle relaxants (+, excitatory effect; –,inhibitory effect; α-motor neuron; E, excitatory interneuron; I, inhibitory interneuron)[13]

Table 3.7: Commonly used muscle relaxants

Drug name	*Dose (max) PO in mg/ duration*	*Special points*
Baclofen	5–10 (80)/ 8–24 hours	Abrupt withdrawal may predispose to seizures, hallucinations, and increased flexor spasm
Tizanidine	4–8 (36)/ 12–24 hours	More effective in reducing muscle spasm but less consistent in decreasing muscle tone. Careful administration when used with other antihypertensive
Diazepam	2–4 (20)/ 12–24 hours	Concomitant use of other centrally acting drugs may potentiate side effects
Thiocolchicoside	4–8/ 12 hours	Act predominantly via supraspinal level activity, along with myorelaxant also has anti-inflammatory and analgesic actions.
Dantrolene	25 (400)/ 12 hours	Not indicated for skeletal muscle spasm or pain of rheumatologic origin

topical. Steroid relieve pain by reducing inflammation and blocking transmission of nociceptive C fiber input.

Though epidural and intra-articular steroid are frequently used in pain management scope of oral steroid is limited. Mostly oral steroids are used in systemic diseases like acute rheumatoid arthritis or spondyloarthopathies, or in bone pain due to metastatic cancer.

Long-term and systemic steroid administration definitely have more serious side effects like suppression of hypothalamic pituitary adrenal axis, osteoporosis, metabolic changes, hyperglycemia.

Particulate steroids are preferred over soluble preparations in pain procedures. Commonly used preparations are methylprednisolone acetate, triamcinolone acetate, triamcinolone diacetate. Orally used steoids are prednisolone, betamethasone, deflazacort, methylprednisolone.

NMDA Receptor Antagonist

NMDA receptors are involved in 'wind up' phenomenon, modulation of pain pathway and hyperalgesia. Thus inhibition of these can have potent analgesic effect.

Ketamine is popular one in this group though oral preparations not available. Parenteral ketamine used in central sensitized conditions like fibromyalgia. Also used in opioid tolerance, CRPS, phantom limb pain, opioid induced hyperalgesia.

α_2 Agonists

These drugs have a sympatholytic effect and they also alter calcium and potassium conductance at spinal cord level. Commonly used one is clonidine (dose 0.1 mg/day orally). It is useful in sympathetically mediated neuropathic pain conditions like CRPS.

Local Anesthetics

Local anesthetics drugs like lignocaine and bupivacaine are used to block nerves as a diagnostic or therapeutic procedure.

Systemic lignocaine administration done I central desensitization procedure, there it acts as a membrane stabilizer.

Botulinum Toxin

Pain associated with spasticity, myofascial pain, cervical dystonia, some headache disorder respond well to therapeutic botox injection. It acts on the neuromuscular junction, analgesic action probably mediated by blockade of substance P, glutamate, and calcitonin gene related peptide.

Topical Agents

- There are many topical agents which are used in pain management. Like topical analgesic gels, capsaicin, EMLA cream.
- Topical NSAIDs are very popular but it has limitations like systemic absorption and only applicable to small areas. Total drug

Table 3.8: Summary—medication classes useful in chronic pain[2]

Drug class	*Pain treated*
Opiates (oxycodone, tramadol, hydrocodone, morphine methadone)	Used for nociceptive pain; helpful with appropriate adjuvants for neuropathic pain.
NSAIDs (aspirin, naproxen, ibuprofen, celecoxib)	Mainly useful for nociceptive pain; the COX-2 inhibitors have increased the variety of clinical settings where they can be used reduced GI discomfort.
TCAs (amitriptyline, nortriptyline, doxepin, imipramine)	Neuropathic pain, can improve sleep mood.
SNRIs (duloxetine, venlafaxine)	Act on both serotonergic as well as noradrenergic pathways. Lesser side effect than TCA.
SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	Some studies have suggested that these might be helpful in neuropathic pain syndromes. They are helpful for depression, which is common in chronic pain.
Anticonvulsants (gabapentin, pregabalin, tegretol, valproic acid, valium, topiramate, levetiracetam, zonisamide, lamotrigine)	Primarily used for neuropathic pain syndromes; can be useful as adjuvant for opiates and improvement in quality of sleep.
NMDA receptor antagonists (ketamine, memantine dextromethorphan)	Useful as opiate adjuvants, might help to improve responsiveness of neuropathic pain to opiates; might be helpful to manage opiate tolerance
Muscle relaxants (baclofen, valium, cyclobenzaprine)	Myofascial pain form muscle spasms and headaches.
μ-2 agonists (tizanidine, clonidine)	Useful for opiate withdrawal, can be helpful for neuropathic pain division line.
Topical medications (lidocaine patch, capsaicin)	Localized neuropathic pain or dysesthesias.

amount is also difficult to monitor. Thus prolong use of topical diclofenac or other NSAIDs should be avoided.

- Capsaicin, a vannilloid receptor agonist, is derived from cayenne pepper. It works by depleting substance P in nerve terminals. 0.025 to 0.075% cream to be applied 2–4 times a day.
- Anesthetic patches are indicated in PHN and other neuropathic pain. Topical anesthetics are required for occlusive dressing in painful conditions.

REFERENCES

1. McmohanS, Koltzenberg M editors. Wall and Melzack's textbook of pain. 5th ed. London: Churchill Livingstone; 2006.p371–552.
2. Dinakar P, Ross EL. multidisciplinary approach to chronic pain management. In Vacanti CA, Sikka PK, Urman RD, Dershwitz M, Segat BS editors. Essential clinical anesthesia. 1st ed. New York: Cambridge university press; 2011. p894–900.
3. Dureja GP,Iyer RN,Das G,Ahdal J,Narang P. Evidence and consensus recommendations for

the pharmacological management of pain in India. Journal of Pain Research 2017:10 709–36.

4. Gehdoo RP. Cancer Pain Management. Indian J Anaesth. 2006;50(5):375–90.
5. Ross EL. Pain Management. Hot Topics. 1st ed. Philadelphia: Hanley and Belfus; 2003.
6. Rosenquist RW, Vrooman BM. chronic pain management. In:Butterworth JF, Mackey DC, Wasnick JD editors. Morgan and Mikhail's Clinical anesthesiology. 5th ed. New Delhi: McGraw hill education (India);2014.p 1023–88.
7. Dureja GP. Handbook of pain medicine. 2nd ed. New Delhi: Elsevier; 2014.p 59–96.
8. Sood J. Pharmacology of pain. In: Joshi M editor. Textbook of pain management. 3rd ed. Hyderabad: paras medical publisher;2014.p 71–90.
9. Tripathi KD. Essential of medical pharmacology. 6th ed. New Delhi: Jaypee;2008.
10. Burkey DR, Fleisher L A editors. Regional anesthesia and pain management. 1st ed. Philadelphia: Saunders; 2009.p 103–22.
11. Waldman SD editor. Pain management. 2nd ed. Philadelphia: Saunders; 2011.p 878–945.
12. Benzon, Rathmell, Wu, Turk, Argoff editors. Raj's practical management of pain. 4th ed. Philadelphia: Mosby Elsevier.2008.p 597–713.
13. Fishman SM, Ballantyne JC, Rathmell JP, editors. Bonica's management of pain. 4th ed. Philadelphia: Lippincott Williams & Wilkins.2009. p1153-1260.

CHAPTER

4

Psychological Aspects of Chronic Pain

Ayananshu Nayak and Kanchan Sharma

"A common misconception is that pain is a purely physiological phenomenon. In fact, "pain" represents a final integrative package, the components of which consist of neurophysiological processes as well as contextual, psychological as well as sociocultural factors"[1]

Pain is a subjective feeling and every individual at some point of their life would have suffered from it. Chronic pain is associated with high direct costs to all the healthcare systems in particular and indirectly to the whole society in general with lost productivity[2]. There is of course considerable impairment of mood, functional abilities and quality of life that come with chronic pain.[3]

Neuroscience of pain: Studies[4–7] show that pain results in the activation of primary and secondary somatosensory cortex which are responsible for the sensory-discriminative aspects of pain. On the other hand, activation of anterior cingulate cortex, prefrontal cortex, insular cortex, thalamus, amygdala and nucleus accumbens results in the affective component of pain.

PSYCHOPATHOLOGY AND EPIDEMIOLOGY

Chronic pain and many affective or stress-related conditions share similar personal risk factors. For instance, childhood adversity is linked to both conditions developing later in life. More than two-thirds of people suffering from chronic pain will have clearly demonstrable psychopathology and more than half would be sufficiently severe to attract formal diagnoses of mental illnesses requiring treatment. The most commonly reported association of chronic pain is with depression and has been extensively studied.[8–16] Prevalence of depression in patients with chronic pain is reported to be between 18 and 85% depending on the conducted survey,[14–15] whilst the prevalence of chronic pain in patients treated for depression is reported to be between 51.8 and 59.1%[9–11]. Various studies[17–21] have been conducted to find out the effect of duration, severity, response to treatment, and family and social interactions of chronic pain and depression. Pain has other affective components such as anxiety, sadness, unpleasant mood, disturbed sleep, irritability, decreased concentration, loss of appetite, etc.[22, 23] Indeed generalised anxiety disorder is reported to be one of the most common associations of chronic pain.[24] Other common associations are post-traumatic stress disorder, substance misuse disorders (often iatrogenic), psychosexual issues as well as obesity and other eating disorders. Loosely defined somatoform pain disorder contributes significantly (12–19%) to the overall lifetime prevalence of pain burden in any society.

Assessment

Effective screening tools have been devised to identify psychological conditions. They help us in screening the patients' psychological status but should play little role in formal diagnosis. A routine screening for depression should be

made for two important reasons: one, this is likely to be the most common comorbidity of chronic pain and imposes heavy burden of overall morbidity but second and more importantly, failure to address depression often results in poor satisfaction with the treatment[25] of chronic pain itself and higher overall cost of treatment.[26]

The UK National Institute for Health and Clinical Excellence (NICE) in 2009 recommended using the following two questions to screen for depression:

1. During the last month have you been feeling down, depressed or hopeless?
2. During the last month have you often been bothered by having little interest or pleasure in doing things?

The sensitivity and specificity of these two questions has been found to be over 95% and between 75 and 85% respectively.[27]

Following scales help us in the mental assessment of the chronic pain patients:

PHQ-9 Scale[28]

It consists of 9 questions and they have their answers in the respective columns as "not at all" which corresponds to 0, "several days" which corresponds to 1 "more than half the days" which corresponds to 2 and, "nearly everyday" which corresponds to 3. We need to add together column scores to get a total score. The interpretation of total score and severity of depression is as follows: 0–4 none, 5–9 mild, 10–14 moderate, 15–19 moderately severe, 20–27 severe.

Beck Depression Inventory (BDI)[29]

This have 21 parameters and each are graded from 0 to 3 thus have total score of 63. Result will be inferred as below:

- 1–10—ups and downs are considered normal.
- 11–16—mild mood disturbance.
- 17–20—borderline clinical depression.
- 21–30—moderate depression.
- 31–40—severe depression.
- > 40—extreme depression.

Hamilton Depression Scale [29,30]

It includes 17 parameters with score grade of 0 to 4 (symptom is absent, mild, moderate or severe) thus total score of 54.

	Not at all	*Several days, but less than half a month*	*Nearly days, more than half a month*	*Nearly everyday*
A. Little interest or pleasure in doing things	0	1	2	3
B. Feeling down, depressed or hopeless	0	1	2	3
C. Trouble falling or staying asleep or sleeping too much	0	1	2	3
D. Feeling tired or having a little energy	0	1	2	3
E. Poor appetite or overeating	0	1	2	3
F. Feeling bad about yourself or that you are a failure or have let yourself or your family down	0	1	2	3
G. Trouble concentrating on things such as reading the newspaper or watching television	0	1	2	3
H. Moving or speaking so slowly or so restlessly that other people could have noticed	0	1	2	3
I. Thoughts that you would be better off dead, or thoughts of hurting yourself in some way	0	1	2	3

PHQ-9 scale

Zung Self-rating Depression Score [29]

It includes 20 parameters with grading ranging from 1 to 4 thus total score of 20–80. Some parameters are given score from 1 to 4 for symptoms increasing in time duration and some are given in reverse.

Hospital Anxiety and Depression Scale (HADS)[31]

It includes 14 parameters with 2, 4, 6, 8, 11, 12, 14 for anxiety and 1, 3, 5, 7, 9, 10, 13 for depression. Scoring is done as 3, 2, 1, 0 (for item 7 and 10 scoring is reversed). Score of 0–7 indicates non case; 8–10 indicate borderline case and 11 or above indicate case. This scale is specifically designed for use in physically unwell patients and is likely to be more suitable in chronic pain settings compared to other available scales and screens for anxiety in addition to depression.

Pain catastrophizing scale (PCS)[32] and the **Tampa scale of kinesophobia**[33] helps inassessing personality disorder.

Management

Long-term or high dose use of NSAIDS and opiates should be discouraged in chronic pain. Instead, their use should only be to tide over crises. Self-help and coping strategies such as healthy living should be encouraged. An empathic primary care physician is often the most effective messenger who underscores and highlights the degree of autonomy and control that most patients usually still retain despite difficult pain symptoms. A general practitioner also must undertake the arduous task of providing basic elements of solution focussed therapy, i.e. jointly exploring practical solutions to common daily difficulties that their patients face.

It is vital to locate a psychiatrist trained to deal with patients suffering from chronic pain symptoms who is prepared for the hard and sometimes excruciatingly slow progress in this field. Close liaisons between the different clinicians is a basic necessity of any treatment service where the primary care physician plays a central role and coordinates efforts of every other clinician. Of course, stigma remains a challenge everywhere. The clinicians must be honest in explaining that he or she is duty bound to explore every possibility of success. Usually patients are receptive to the suggestion of treatment for psychological reaction to their pain symptoms.

Some psychotropic medications are useful in neuropathies. However, their mechanism and sites of action in neuropathic pain are independent of their efficacy as psychotropics. One must not confuse these two roles. For instance, perception of pain subsides with the use of amitriptyline at times. This effect has no relation to its antidepressant efficacy. Indeed, routine use of antidepressants in chronic pain and for chronic pain is pointless and is discouraged in all the standard guidelines. These medicines should be used with caution but they may be of great help when used appropriately. More recently, use of cannabidiol and ketamine have been used in experimental settings to treat chronic pain as well as some mental health comorbidities and show some promise. However, more research should confirm their safety and efficacy before routine clinical use could be recommended.

Use of talking treatments for chronic pain is now established, cost-effective, clinically well studied and evidence-based practice. (ref: british pain society guidelines 2013) When initiated in the specialist settings by well trained therapists, various forms of talking treatments produce consistently reliable if relatively small beneficial effects. Newer forms of therapies show more promising results. A psychiatrist should be involved in the decision to screen patients for thorough assessment before a particular type of therapy is chosen.

REFERENCES

1. Cohen, et al; BMJ 2014: 348f7656.
2. Phillips, et al. BJ Pain, 2009.
3. Nickel R, Raspe HH.Chronic pain: Epidemiology and health care utilisation. Nervenarzt 2001; 72:897–906.
4. Schweinhardt P. Bushnell MC. Neuroimaging of pain: insights into normal and pathological pain mechanisms. Neuroscience Letters. 2012; 520(2):129–30.
5. Apkarian AV Bushnell MC, Treede RD. Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. European Journal of Pain. 2005;9(4):463–84.
6. Tracey I, Johns E. The pain matrix: reloaded or reborn as we image tonic pain using arterial spin labelling. Pain. 2010;148(3):359–60.
7. Bushnell MC, Čeko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. Nature Reviews Neuroscience. 2013;14(7):502–11.
8. Demyttenaere K,Bruffaerts R,Lee S,Posada-Villa J, Kovess V, Angermeyer MC, et al. Mental disorders among persons with chronic back and neck pain: Results from the World Mental Surverys: Pain 2007;129:332–42.
9. Von Knorring L, Perris C, Eisemann M, Eriksson U, Perris H. Pain as a symptom in depressive disorders. II. relationship to personality traits as assessed by means of KSP. Pain. 1983;17(4): 377–84.
10. Lee P, Zhang M, Hong JP, et al. Frequency of painful physical symptoms with major depressive disorder in Asia: relationship with disease severity and quality of life. Journal of Clinical Psychiatry. 2009;70(1):83–91.
11. Agüera-Ortiz L, Failde I, Mico JA, Cervilla J, López-Ibor JJ. Pain as a symptom of depression: prevalence and clinical correlates in patients attending psychiatric clinics. Journal of Affective Disorders. 2011;130(1-2):106–12.
12. Gureje O, Simon GE, Von Korff M. A cross-national study of the course of persistent pain in primary care. Pain. 2001;92(1-2):195–200.
13. Carroll LJ, Cassidy JD, Côté P. Depression as a risk factor for onset of an episode of troublesome neck and low back pain. Pain. 2004;107(1–2): 134–9.
14. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. Archives of Internal Medicine. 2003; 163(20):2433–45.
15. Williams LS, Jones WJ, Shen J, Robinson RL, Weinberger M, Kroenke K. Prevalence and impact of depression and pain in neurology outpatients. Journal of Neurology, Neurosurgery and Psychiatry. 2003;74(11):1587–9.
16. Hilderink PH, Burger H, Deeg DJ, Beekman AT, Oude Voshaar RC. The temporal relation between pain and depression: results from the longitudinal aging study Amsterdam. Psychosomatic Medicine. 2012;74(9):945–51.
17. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. Clinical Journal of Pain. 1997;13(2):116–37.
18. Gerrits MMJG, Vogelzangs N, Van Oppen P, Van Marwijk HWJH, Van Der Horst H, Penninx BWJH. Impact of pain on the course of depressive and anxiety disorders. Pain. 2012;153(2):429–36.
19. Bair MJ, Robinson RL, Eckert GJ, Stang PE, Croghan TW, Kroenke K. Impact of pain on depression treatment response in primary care. Psychosomatic Medicine. 2004;66(1):17–22.
20. Dworkin RH, Gitlin MJ. Clinical aspects of depression in chronic pain patients. Clinical Journal of Pain. 1991;7(2):79–94.
21. Ohayon MM, Schatzberg AF. Chronic pain and major depressive disorder in the general population. Journal of Psychiatric Research. 2010;44(7):454–61.
22. Gureje O, Von Korff M, Kola L, Demyttenaere K, He Y, Posada-Villa J, et al. The relation between multiple pains and mental disorder:Results from the World Mental Health Surveys. Pain 2008; 135:82–91.
23. Chaturvedi SK, Rao GP, Sarda KD, Suryawanshi SY. Chronic pain and depression: An online survey on Indian experiences.Indian J Pain 2014;28:166–72.
24. Polatin PB, et al. Spine (Phila Pa 1976). 1993 Jan;18(1):66–71.

25. Predicting poor outcomes for back pain seen in primary care using patients' own criteria. Cherkin DC, Deyo RA, Street JH, Barlow W.Spine (Phila Pa 1976). 1996 Dec 15;21(24):2900-7.
26. Engel, et al. Pain, Volume 65, Issues 2–3, May–June 1996, Pages 197–204.
27. Arroll B, et al. BMJ Nov.2003;pp:1144–6.
28. Kroenke K, Spitzer R, Williams W. The PHQ-9: Validity of a brief depression severity measure. JGIM, 2001,16:606–16.
29. Cusin C, Yang H. Rating scales for depression. In: Baer L, Blais MA (Eds). Handbook of Clinical Rating Scales and Assessment in Psychiatry and Mental Health. New York: Humana Press; 2010.
30. Lopez-Pina JA, Sanchez-Meca J, Risa-Alcazar AI. The Hamilton rating scale for depression: a meta-analytic reliability generalisation study. Int J Clin Health Psychol 2009;9:143–59.
31. Bjelland I, Dahl AA, Haug TT, et al. The validity of the hospital anxiety and depression scale, an updated literature review. J Psychosom Res 2002;52:69–77.
32. Sullivan MJ. The Pain Catastrophizing Scale User Manual. Montreal, 2009.
33. Burwinkle T, Robinson JP, Turk DC. Fear of movement: Factor structure of the Tampa Scale of Kinesophobia in patients with fibromyalgia syndrome. J Pain 2005;6:384–91.

CHAPTER

5

Myths in Pain Management

Sunita Lawange

There are many myths about various painful conditions and their treatment. New researches have proved that these are mere myths and not facts. In this chapter we shall discuss about some common myths and the facts.

Myth: NSAIDs (non-steroidal anti-inflammatory drugs) are the drug of choice for every kind of pain including chronic pain.

Fact: NSAID are prescribed for almost every kind of pain, and they are the most commonly used over the counter drugs. But before prescribing them we should have knowledge about the type of pain and character of pain. NSAIDs should be prescribed only for nociceptive type of pain specially when there is an inflammatory component. Most of the time, sensitization develops in chronic pain and NSAIDs are going to have a limited role. Moreover, NSAIDs should not be prescribed for chronic use, because of their side effects. Paracetamol, opioids and co-analgesics like antidepressant and anticonvulsants have got a better role to play in chronic pain.[1,2,3]

Myth: If a patient is on opioid for a long time, addiction follows successively.

Fact: Addiction is characterized by compulsive drugs seeking behaviour and compulsive use of drug, despite of harmful consequences. However, dependence is characterized by the need of a drug by the person to function normally and abruptly stopping the drug leads to withdrawal symptoms. Opioids form a part of treatment for chronic pain. If it is prescribed for a short duration, the risk of development of addiction is minimal. Also in some opioids like tramadol, fentanyl, etc. addiction is very rare.[4]

Myth: Bed rest for 3 to 4 weeks is the best and easiest treatment for acute back pain.

Fact: When the stability the spine is at risk and in presence of other red flags bed rest may be advisable. In all other situations more than 3 days bed rest is not advisable. Bed rest reduces muscle mass, increases osteoporosis, enhances disc degeneration, increases chance of other complications like hypostatic pneumonia, deep vein thrombosis, etc. Thus within the limitations of pain, patients should be allowed and encouraged to do his/her daily life activities.[5, 6]

Myth: When we are not able to diagnose the cause of pain by different modern imaging, it must be psychological.

Fact: Image can show us the structural abnormalities. But some structural abnormalities may not produce pain and in some kinds of pain no structural abnormalities are observed. WHO states that chronic pain is a disease itself and must be treated. Pain if presents for a long time affective components manifest in the form of the anxiety, depression, sadness, mood disorder, disturbed sleep, irritability, decreased concentration, loss of appetite, etc. We should be specially trained to distinguish between the two things:

Whether the chronic pain is the manifestation of depression or depression is manifestation of chronic pain. Certain conditions like fibromyalgia all tests might come normal.[7–9]

Myth: Pain medications should be taken only when pain is severe and unbearable.

Fact: We should start taking the pain medicine even when pain is mild and should not wait it to become moderate to severe. This is to maintain a constant concentration of drug in our body to break the pain cycle and to prevent the development of sensitization. Some pain medications like Duloxetine is slow and effective only after 5–9 weeks.[4,10]

Myth: Investigations like X-rays, CT scan and MRI are mandatory to diagnose chronic pain.

Fact: After ruling out red flags where an extensive investigation and immediate treatment is required, in most chronic pain patients detailed history with a relevant clinical examination is all that is required to arrive to a clinical diagnosis. For example, in case of facet joint and sacroiliac joint arthropathy a diagnostic block with a local anesthetic is required to diagnose them as a source of pain generators rather than the costly investigations like MRI or CT scan. Investigations should be there to support our clinical diagnosis, we should not be treating the reports rather we should train ourselves to treat the disease producing symptoms. For example, an asymptomatic disc prolapse patient needs not to be treated if patient does not have any symptom of that.[10–15]

REFERENCES

1. Yakash TL. Central pharmacology of nociceptive transmission. In: McMahon SB, Koltzenburg M editors. Wall and Melzack's Textbook of Pain. 5th edition. Elsevier Churchill Livingstone; 2006. p.371–414.
2. Watson CPN, ChipmanML, Monks RC. Antidepressant analgesics: a systematic review and comparative study In : McMahon SB, Koltzenburg M editors. Wall and Melzack's Textbook of Pain. 5th edition. Elsevier Churchill Livingstone; 2006.p.481–497.
3. Devor M. Response of nerves to injury in relation to neuropathic pain In : McMahon SB, Koltzenburg M editors. Wall and Melzack's Textbook of Pain. 5th edition. Elsevier Churchill Livingstone; 2006. p. 905–927.
4. Serpell M. Oxford Handbook of Pain Management. Correct Medicine Group. London; 2008. p.6.
5. Deyo RA. Fads in the treatment of low back pain. N *Engl Med 1991;* 325 (14):1039–1040.
6. Waddell G, Feder G, Lewis M. Systematic reviews of bed rest and advice to stay active for acute low back pain. Brit Gen Pract 1997;47:647–652.
7. Gureje O, Von Korff M, KolaL, Demyttenaere K, HeY, Posada-Villa J,et al. The relation between multiple pains and mental disorder: Results from the World Mental Health Surveys. Pain 2008;135:82–91.
8. Von Knorring L, Perris C, Eisemann M, Eriksson U, Perris H. Pain as a symptom in depressive disorders. II. Relationship to personality traits as assessed by means of KSP. *Pain*.1983; 17(4): 377–384.
9. Lee P., Zhang M., Hong J. P., et al. Frequency of painful physical symptoms with major depressive disorder in Asia: Relationship with disease severity and quality of life. *Journal of Clinical Psychiatry*. 2009;70(1):83–91.
10. Spitzer WO, LeBlanc FE, Dupuis M, et al. Scientific approach to the activity assessment and management of activity-related spinal disorders. *Spine*. 1987;12(7):S1–S55.
11. Hancock MJ, Maher CG, Latimer J, et al. Systematic review of tests to identify the disc, SIJ or facet joint as the source of low back pain. *EurSpine J*. 2007;16(10):1539–1550.
12. Seffinger MA, Najm WI, Mishra SI, et al.Reliability of spinal palpation for diagnosis of back and neck

pain: A systematic review of the literature. *Spine*. 2004;29 (19): E413–E425.

13. Boos N, Rieder R, Schade V, Spratt KF, Semmer N, Aebi M. 1995 Volvo Award in clinical sciences. The diagnostic accuracy of magnetic resonance imaging, work perception, and psychosocial factors in identifying symptomatic disc herniations. *Spine*. 1995;20(24):2613–2625.7
14. Van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Spinal radiographic findings and nonspecific low back pain. A systematic review of observational studies. *Spine*. 1997;22(4):427–434.
15. Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. *J Bone Joint Surg Am*. 1990;72A:403–408.

SECTION

II

Back Pain Management

Samarjit Dey and Palak Mehta (Section Editors)

6. Pain Generators in the Back
7. Evaluation of Patient with Back Pain
8. Management of Back Pain
9. Myths in Back Pain

CHAPTER

6

Pain Generators in the Back

Rammurthy

As low back pain is one of the common complaints seen in outpatient service ward, it is mandatory to have some basic knowledge on lumbosacral spine anatomy and its pain generators. It also helps in understanding the pathophysiology of the various disease processes that may cause back pain.

The Lumbar Vertebra

There are 5 lumbar vertebrae, articulated with each other by intervertebral discs anteriorly and facet joints posteriorly with forward lordotic curve. Each vertebra has two pedicles projecting posteriorly, two transverse processes, a pair of superior and inferior articular processes, a pair of lamina and one spinous process.[1] Each vertebra is divided into three functional components namely the vertebral body(anterior element), the pedicle with intervertebral foramen (middle element) and lamina and its processes (posterior element) (Fig. 6.1).

It is supported by various ligaments like anterior and posterior longitudinal ligaments which are present on the anterior and posterior surface of the vertebral body and the disc, interspinous ligament which is present between the two consecutive spinous processes, supraspinous ligament which connects tip of two spinous processes and ligamentum flavum which connects the laminae of consecutive vertebrae[2] (Fig. 6.2). The lumbar spine is strengthened by numerous paraspinal muscles which include the spinalis, longissimus, quadratus lumborum, iliopsoas, iliocostalis. These muscles stability as well as mobility to the spine.

In between the anterior and posterior elements is spinal canal which contains spinal cord surrounded by vertebral body and

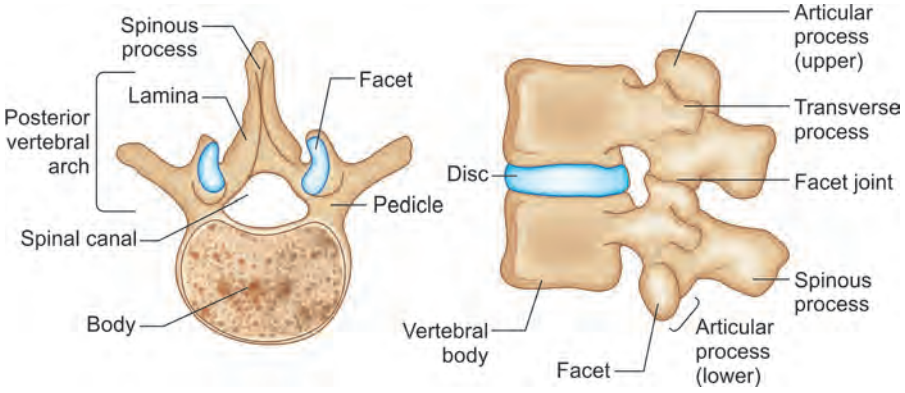


Fig. 6.1: Lumbar vertebra

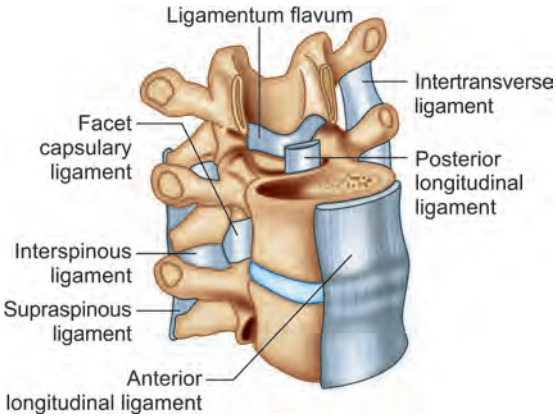


Fig. 6.2: Ligaments covering lumbar vertebra

intervertebral disc anteriorly, pedicle and vertebral foramen laterally and lamina with ligamentum flavum posteriorly.[1]

Since lumbar spine is surrounded by multiple muscles and there are many viscera near by, it becomes a challenge for the clinician to identify the pain generator in case of low back pain. Hence the history and physical examination is important in identifying the pain generators.

Anterior element is supplied by sympathetic chain and sinuvertebral nerve which again is a part of grey rami communicants.[3] Posterior element is supplied posterior rami of spinal nerve which again has three branches namely medial, intermediate and lateral (Fig. 6.3). All anterior and posterior elements have nerve supply except inner 2/3rd of annulus fibrosus and nucleus pulposus of intervertebral which are the potential pain generators.

Sacrum and Coccyx

Sacrum is a single triangular or wedge shaped bone formed by the fusion of 5 sacral vertebrae. It articulates with the L5 vertebra above. It also articulates with the right and left iliac bones to form right and left sacroiliac joints. The sacrum has 4 anterior and 4 posterior sacral foramina through which the anterior and posterior rami of the upper four sacral spinal nerves exits. The sacro-iliac joint is a diarthrodal joint but only anteroinferior part of the joint is synovial. The sacroiliac joints are designed primarily for stability.

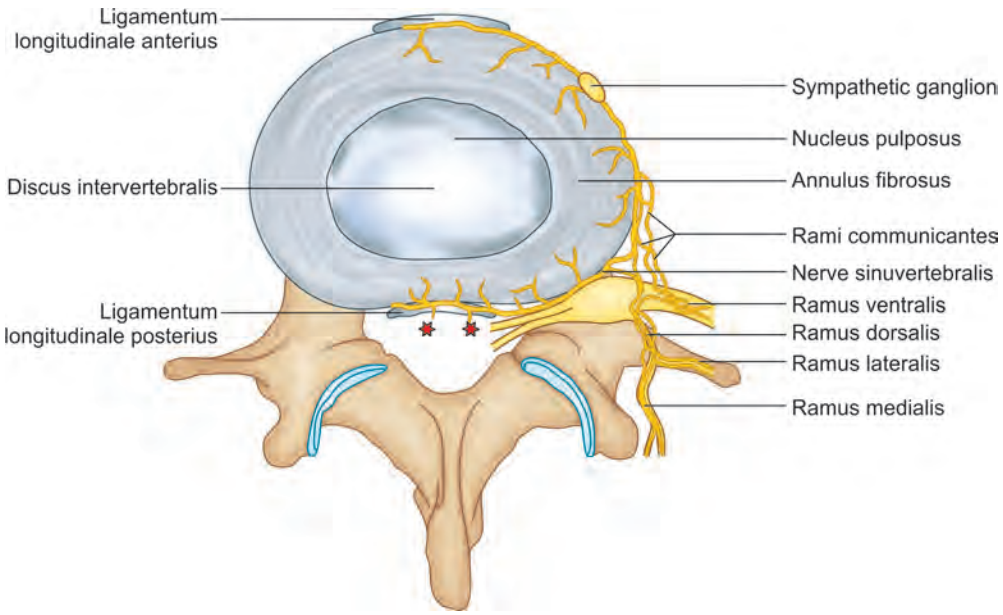


Fig. 6.3: Lumbar spine and nerve supply

Their functions include the transmission of the truncal load to the lower limbs. The sacroiliac joint is largely immobile and is maximally loaded while sitting.

Coccyx, also called tail bone is formed by fused 3–5 coccygeal vertebrae. It is articulated to the sacrum by sacrococcygeal joint and sometimes can be mobile (Fig. 6.4). The spinal cord ends at the level of lower border of L1 but the dural sac continues till the level of S2.[1] The spinal nerve roots exit the spine via the intervertebral foramen. Each nerve root exits below the corresponding vertebra.

Pain Generators in Lower Back

To be a pain generator or source of pain an anatomical structure must have a nerve supply. In back the following structures can be a source of pain:

1. Intervertebral disc
2. Facet joint
3. Sacroiliac joint
4. Skeletal muscles
5. Vertebral body
6. Dura
7. Bursae
8. Ligaments
9. Hip joint

Internal disc disruption: When the disc is degenerated, the inner layers of annulus are affected as it don't have blood supply. Thus, the boundary wall is weakened and nucleus starts leaking and comes within the layers of annulus. In an attempt to heal the inner layers of annulus, the blood vessels from outer one third of annulus start growing inside accompanied by sympathetic nerves.

Glycoprotien molecules are segregated from body's immune system from fetal life, so when they comes in contact with blood vessels body recognizes these glycoprotiens as foreign materials and there will be inflammatory reacotions. Finally sympathetic nerves are also inflammed and sensitized. Thus, any rise of intradiscal pressure irritates sensitized sympathetic nerves and creates pain. Here the pain generators are sympathetic nerves inside the disc, so patient feels predominent back pain which is deffuse, poorly localized and non-dermatomal in distribution. Sitting agravates pain as sitting increases inra-discal pressure.

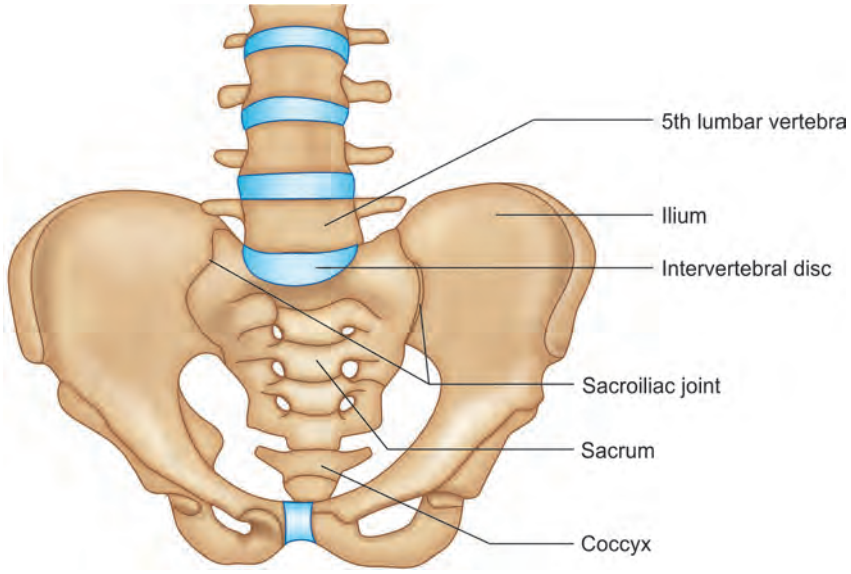


Fig. 6.4: Pelvic bones

Disc prolapse: When nucleus pulposus leaks further, it comes in contact with the nerve roots and produce inflammation and/or mechanical compression. So patient feel leg pain along the compressed/inflamed nerve root with or without sensory/motor deficits. Pain increases on walking.

Intervertebral Disc

Disc have three parts, annulus, nucleus and end plates. Only outer one-third of annulus have blood supply and accompanying sympathetic nerves. Rest inner two-third and whole of the nucleus don't have any blood or nerve supply. The blood vessels comes from lumbar segmental arteries and nerves comes from gray rami communicants. Intervertebral discs don't have any somatic nerves.

Nucleus pulposus is a jelly like substance having 80% water. This water is retained inside the disc because of high osmotic pressure provided by high molecular weight glyco-proteins mostly aggrecans. The glyco-proteins are synthesized by chondrocyte cells inside the nucleus. Presence of water inside the disc is the balance of two opposite force, osmotic pressure which tries to hold water inside disc and intradiscal pressure which tries to force water out of disc. At night our disc swells with more water as intradiscal pressure is very low at lying down position at night. When we grow older, number of chondrocyte cells are reduced, manufacturing less glyco-proteins and less water in nucleus. Thus disc looks dehydrated on MRI and flexibility of spine is reduced. This is called aging of disc which affects nucleus.

Annulus serves few important functions. It is a tough fibro-cartilaginous structure having 15–25 layers called lamellae which stands like boundary wall and gives the disc height. If disc height is reduced, there will be loading of facet joints and neural foraminal size is also reduced. Second important function of annulus is to provide oxygen and nutrients to the whole of the disc as it don't have any blood supply. This process is facilitated by fluctuation of intra-discal pressure. Thus, prolonged bed rest is harmful as it keeps disc pressure continually at low level. While sitting change of posture is important to keep intra-discal pressure fluctuating. Third important function of annulus is to hold gel like nucleus pulposus inside and not allowing it to leak.

Facet Joint

Facet joint is a synovial joint formed by superior articular process from below and inferior articular process from above. It is innervated by two medial branches, one from of dorsal rami of same level nerve root and another from above level. These are somatic nerve so facet pain is well localized. Facet joint is loaded by extension, lateral bending and rotation. So these movements increases pain. On the other hands, forward bending unloads facet joints and it reduces facet pain. Thus sitting relieves pain from facet origin.

Facet pain is predominantly felt at back and usually not associated with any neuro-deficits except facet cysts.

Sacroiliac Joint

Sacroiliac (SI) joint is a large joint having a synovial part in lower and anterior part and a fibrous part in posterior and superior part. It is innervated by lateral branches of dorsal rami of Sacral 1-2-3 nerve roots. But nerve supply also comes from L4, L5, S4 also. SI joint is loaded when we sit, or stand for longer time. So SI joint pain is aggravated on sitting. It is also not associated with neuro deficits.

Skeletal Muscles

There are many skeletal muscles in lower back and buttock which can be a pain generator. When skeletal muscle is source of pain, it is known as myofascial pain. There will be contractile bands in the muscle and some sensitized zone known as trigger point. On pressing trigger point pain radiates distally and there is visible contraction of the muscle known as jump sign. As muscle remains contracted, the contracted band may compress

nearby nerves which may mimic radicular pain.

Myofascial pain of few muscles thus may mimic sciatica. These are Psoas muscle, Quadratus lumborum muscle which forms the anterior and posterior boundary of lumbar plexus. Same way piriformis muscle is just posterior to sciatic nerve and may produce sciatica.

Vertebral Body

This is also innervated by sympathetic nerves in the same way like disc. Thus the pain will be defuse without radiation. Vertebral body can be a pain generator when it is fractured or have metastasis. Pain increases on sitting and standing.

Dura

When dura is pushed by bulging disc or by ligamentum flavum, there may have diffuse back pain without radiation.

Bursae

There are several bursae around hip and in pelvis which can be the pain generators.

Ligaments

Ligaments around lower back, and pelvis are pain generators at times.

Hip Joint

Hip joint pathologies must be ruled out in lower back pain. It can be pain generator in some situations.

Conclusion

Whenever we start examining a patient with low back pain, we should immediately think of pain generators. Some of these may be dangerous also called red flags. We should take detailed history, step by step clinical examinations and appropriate investigations to make final diagnosis and rule out differential diagnoses.

REFERENCES

1. Das G, Gurumoorthi R. Common pain management procedures—video book. Volume 1. Kolkata: Daradia The pain clinic; 2013.
2. Bogduk N. Clinical anatomy of lumbar spine and sacrum. Elsevier; 2005.
3. Raj PP. Intervertebral Disc: Anatomy–Physiology–Pathophysiology—Treatment. Pain Practice. 2008; 8(1):18–44.

CHAPTER

7

Evaluation of Patient with Back Pain

Rammurthy

International Association for the Study of Pain (IASP) defines lumbar spinal pain as pain perceived anywhere within a region bounded by the last thoracic spinous process, the first sacral spinous process and the lateral border of erector spinae. Sacral spinal pain is defined as pain perceived anywhere in a region bounded by first sacral spinous process, posterior sacrococcygeal joints and the posterior superior iliac spines. Low back pain is defined as lumbar spinal pain or sacral spinal pain or any combination of the two.[1] Low back pain is also defined as pain and discomfort, localised below the costal margin and above the inferior gluteal folds, with or without leg pain.[2]

History

Duration[2,3]

Low back pain can be classified depending on the duration into:

1. **Acute low back pain:** Low back pain persisting for less than 6 weeks.
2. **Sub-acute low back pain:** Low back pain persisting between 6 and 12 weeks
3. **Chronic low back pain:** Low back pain persisting for 12 weeks or more.

Pain generator may change as the pain becomes chronic and longstanding. For example, in case of acute lumbar disc prolapse, the pain generator is the inflamed, irritable nerve root generating the ectopic signals. But as the pain becomes long-standing (without treatment), due to sensitization of the nervous system, the pain becomes more centralized. It also helps in establishing the treatment plan as the management of acute low back pain and chronic low back pain differs.

Radiation

Low back pain need not be restricted to lumbar and sacral regions. Pain can be referred to other regions, most commonly lower limbs. Referred pain is pain perceived in a region innervated by nerves other than the nerves that innervate the actual source of pain.[3] The upper lumbar facet joint pain may be referred to flanks, hips and lateral thigh, whereas pain from the lower lumbar facet joints are referred to posterior thigh. Facet joint pain is rarely referred below knees[4]. Similarly pain from sacroiliac joint may be referred to lower lumbar region, abdomen, lower limbs and rarely to the foot[5]. Patients with degenerative disc disease (not disc prolapse) have axial back pain which can be referred to anterior thigh (L3–4 disc), lateral thigh (L4–5 disc) and posterior thigh (L5–S1)[6] (Fig. 7.1). Radicular pain due to nerve root irritation caused by herniated disc causes pain radiating along a narrow band which follows a dermatomal pattern (segment of the skin supplied by a single particular nerve root).[7] Same rule applies to the pain caused by herpes zoster. Pain due to entrapment neuropathies follows the distribution of the affected nerves. For example, pain in meralgia paresthetica is seen in distribution of lateral femoral cutaneous nerve (anterolateral aspect of thigh).[8]

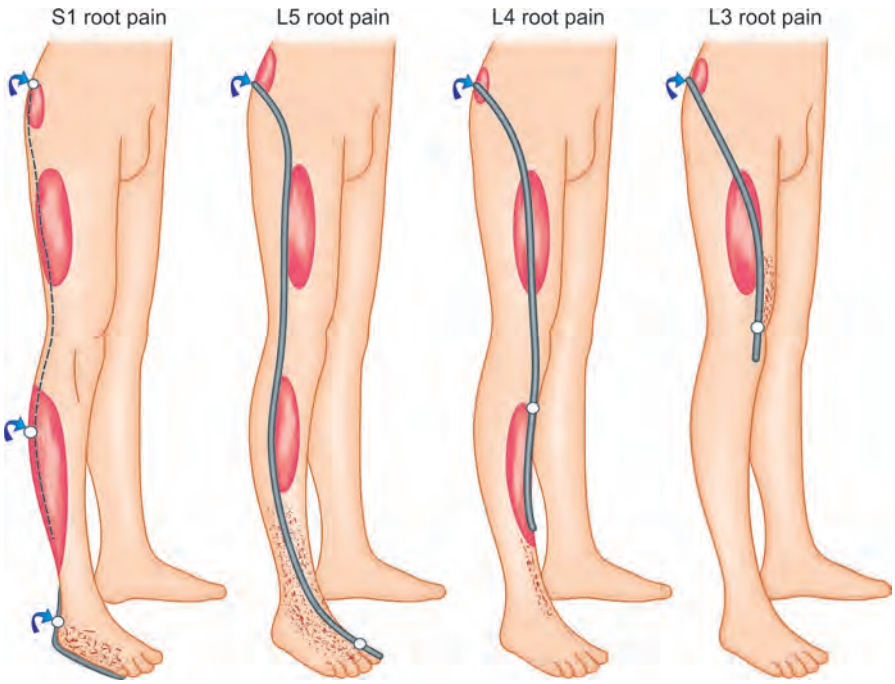


Fig. 7.1: Pain radiation to lower limb according to dermatomes

Quality[9]

Assessing the quality of pain again helps in making the diagnosis. Pain from the facet joints, sacroiliac joints are usually aching types and can be well localized to the area where the pain is originating. Discogenic pain is very vague, and not well localized. Radicular pain and pain due to entrapment neuropathy is sharp, shooting, lancinating or electric in nature.

Intensity

This can be assessed by using standard pain assessment scales—visual analog scale (VAS) or numerical rating scale (NRS). Although it may not help in making the clinical diagnosis, it may aid in selecting the analgesics or invasive treatment.

A. VAS

The pain VAS is a continuous scale comprised of usually 10 centimetres (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom extreme. For pain intensity, the scale is most commonly anchored by "no pain" (score of 0) and "pain as bad as it could be" or "worst imaginable pain" (score of 100).[10]

B. NRS

The NRS is a segmented numeric version of the visual analog scale (VAS) in which a respondent selects a whole number (0–10 integers) that best reflects the intensity of their pain. An 11-point numeric scale (NRS 11) with 0 representing one pain extreme (e.g. "no pain") and 10 representing the other pain extreme (e.g. "pain as bad as you can imagine" and "worst pain imaginable").[10]

Aggravating and Relieving Factors

Lumbar facet joint pain is usually aggravated on backward extension, lateral bending and lateral rotation. The facet joints are loaded during these movements and relieved on lumbar flexion which unloads the joint. Rising in the morning is difficult due to pain and stiffness.[6,11]

Pain of coccidynia is aggravated by sitting and decreased by standing. Hence, the patients frequently use soft cushion or ring to sit and avoid hard surfaces.[12,13] Discogenic pain again increases on axial loading (sitting, lumbar flexion) and reduced by recumbancy.[8] Similarly the pain due to vertebral compression fracture also increases when the patient is sitting. Pain due to ligament sprain and myofascial pain syndrome is aggravated by movements which stretches the affected ligament and muscle. In case of myofascial pain syndrome affecting quadratus lumborum, the pain is worsened in sitting position as the muscle stretched in this position and relieved by standing. Whereas pain of iliopsoas is least in sitting position and aggravated during change of posture from sitting to standing. Pain due to piriformis syndrome is aggravated during squatting which again stretches the piriformis muscle. Similarly, interspinous ligament pain is more while the patient is sitting or bending forwards. Radicular pain is aggravated by bending forwards which stretches the affected nerve, coughing and straining (which increases the intradiscal pressure momentarily) and partial relief is obtain when patient is at rest.[7] Patients with lumbar canal stenosis give a typical history of back pain, numbness and heaviness in the lower limbs while walking which are completely relieved by rest and forward bending.

Red Flags

The most important thing in evaluation of a patient with low back pain is to look for any red flags. Red flags are the danger signs indicating serious underlying condition that needs immediate surgical intervention.

Red Flags for Low Back Pain[2]

1. Trauma—history of major trauma, even minor trauma in elderly patients and patients on long term steroid treatment is considered red flag as they are prone for fractures.
2. Tumor—history suggestive of malignancy like profound weight loss, cachexia, and back pain in a patient already diagnosed with cancer.
3. Infection—history suggestive of infection like fever, weight loss, immunosuppression.
4. Neurological deficits including bladder bowel disturbance and motor power 3/5 or less.

Patients presenting with any of the above signs and symptoms, immediate radiologic assessment and possible surgical interventions within 8 hours or at least before 24 hours.

Psychological Assessment

This is an important part of evaluation as the patients with long standing low back pain will be having emotional disturbances like depression, anxiety, sleep disturbances, loss of appetite.

Clinical Examination

Examination follows the pattern described in the general examination chapter.

Inspection of Back and Leg

Look for asymmetry or deformity; skin lesion, muscle wasting, muscle hypertrophy, muscle fasciculation, gait, posture, range of motion.

Muscle wasting may be sign of motor neuron disease. Gait may be antalgic (painful) gait, steppage gait (due to foot drop) or a gait abnormality due to stiff back as a result of paraspinal muscle spasm. Posture is again a cause for chronic strain on different ligaments.

Range of Motion

The normal ranges of motion of the lumbar spine are 15° of extension, 40° of flexion, 30° of lateral bending, and 40° of lateral rotation to each side.[14]

Palpation

1. Tenderness
2. Swelling
3. Local rise of temperature.

Tenderness over particular part indicates pathology which can extend from superficial skin to underlying organ. In early phase or acute phase of CRPS, the temperature of the affected area is raised; the limb is swollen, edematous, shiny and red. In late or dystrophic phase the skin is cold, atrophic, discolored with loss of hairs.[14] Skin temperature is also reduced and the limb may be cold and discolored in case of vascular pain conditions like Reynaud's disease, Berger's disease and other collagen vascular disorders.

Other important palpatory findings that are important in assessing a patient with pain are allodynia and hyperalgesia.

Motor Testing

Increased muscle tone may be due to spasm of a particular muscle group. Truncal dystonia, stiff person syndrome may be present. Lower limb testing must be included when patient complains of leg pain along with back pain. It is important to predict the site of neural dysfunction.

Power

Each muscle group is to be tested, keeping in mind which root and nerve supply them.

Grade 0	Complete paralysis
Grade 1	A flicker of contraction only
Grade 2	Power detectable only when gravity is excluded by appropriate postural adjustment
Grade 3	The limb can be held against the force of gravity, but not against the examiner's resistance
Grade 4	The limb can be held against gravity and against some resistance, but is not normal (a percentage estimate, or a grade of 4+, 4 or 4– is often applied)
Grade 5	Normal power

Sensory System Examination

Sensory modalities that can be tested includes

- Pain
- Temperature
- Tactile sensibility: This includes light touch and pressure, and tactile localization and discrimination
- Vibration: Place a tuning fork on the malleolus. If deficient, move up to head of fibula or to ASIS.
- Position sense: The appreciation of passive movement. Test with big toe movement.
- Stereognosis: Recognition of the size, shape, weight and form of object.

Reflexes

Deep Reflexes

- ***Knee jerk* (L2,3,4):** The quadriceps contracts when the patellar tendon is briskly tapped. With the patient supine, pass your hand under the knee to be tested so that it supports the relaxed leg with the knee flexed at a little less than 90°. Strike the patellar tendon midway between its origin and its insertion. Look for a contraction of the quadriceps (Fig. 7.2). The knee jerk can often more easily be elicited with the patient sitting up with the legs dangling freely over the edge of the bed.
- ***Ankle jerk* (S1,2):** Slightly dorsiflex the ankle so as to stretch the Achilles tendon and, with your other hand, strike the tendon on its posterior surface, or the sole of the foot. A quick contraction of the calf muscles results.

Superficial Reflexes

- *Cremasteric reflex (L1/2)*. Stroke the skin at the upper inner part of the thigh. The testicle moves upwards.

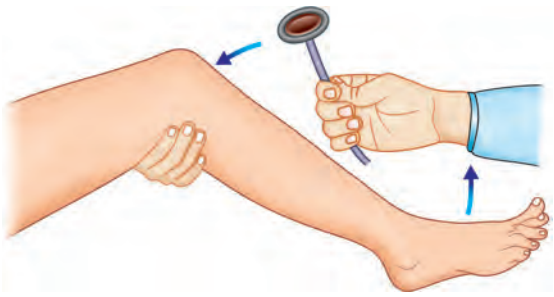


Fig. 7.2: Knee reflex

- *The plantar reflex (L5, S1)*. The outer edge of the sole of the foot is stimulated by firmly scratching a key or a stick along it from the heel towards the little toe. Flexor plantar response is normal.
- *Anal reflex* (S3,4). Gently scratch the skin on either side of the anus. A brisk contraction of the sphincter should immediately occur.
- Bulbocavernosus reflex (S3,4). Pinching of dorsum of glans penis causes contraction of bulbocavernosus.

Special Tests

- The Lasegue straight leg raising test (SLR) for lumbar root irritation:

  The basis for the Lasegue straight leg raising test is the belief that the stretching of the lumbar nerve trunks that form the sciatic nerve is non-painful in healthy but is painful when inflamed, irritated or entrapped. This test also has good correlation with positive findings on magnetic resonance imaging (MRI) of the lumbar spine and lumbar plexus as well as electromyography (EMG). To perform the Lasegue straight leg raising test, the patient is placed in the supine position on the examination table with the unaffected leg flexed to 45° at the knee and the affected leg placed flat against the table. With the ankle of the affected leg placed at 90° of flexion, the examiner slowly raises the affected leg toward the ceiling while keeping the knee fully extended (Figs 7.3 and 7.4). The test is positive if the patient complains of pain and paresthesias into the affected extremity that are similar to the pain that the patient has been experiencing. If this maneuver reproduces the patient's pain, the test may be considered positive.

  The sitting straight leg raising test for lumbar root irritation

  To perform the sitting straight leg raising test, the patient is placed in the sitting position. The examiner then has the patient lean slightly forward to increase tension on

Figs 7.3 and 7.4: SLR test

the lumbar nerve roots. With the ankle of the affected leg placed at 90° of flexion, the examiner slowly raises the affected leg toward the ceiling making the knee fully extended (Fig. 7.5). The test is positive if the patient complains of similar pain and paresthesia into the affected extremity that the patient has been experiencing.

- Tests for sacroiliac joint pain
- The Patrick/FABER test: FABER is an acronym that helps to remind the examiner that he or she is checking for limitation of pain of flexion, abduction and external rotation (FABER). To perform the Patrick/FABER test the patient is placed in the supine position and the knee and hip are flexed to 90°. The examiner then has the patient place the foot of his or her affected extremity on the opposite knee. The thigh is then slowly abducted and externally rotated toward the examination table. (Figs 7.6 and 7.7) Pain will occur in gluteal region near PSIS.

Fig. 7.5: Sitting SLR

Figs 7.6 and 7.7: FABER test

Other tests of interest include

- The distraction test
- Thigh thrust
- Gaenslen's test
- Compression test
- Sacral thrust
- Test for facet joint pain
  - Facet loading test

  In the standing position, patient hyperextends the back and then tries to rotate on either side. Rotation towards the effected side may elicit the pain at a particular point on the back (Figs 7.8 and 7.9). The aim is to stretch the facet joint capsule and thereby producing the pain.
- Test for piriformis syndrome
  - Freiberg's maneuver of forceful internal rotation of the extended thigh elicits buttock pain by stretching the piriformis muscle (Fig. 7.10).

Figs 7.8 and 7.9: Facet loading test

Fig. 7.10. Freiberg's test

- Pace sign, the FAIR test may be performed with the patient in a lateral recumbent position, with the affected side up, the hip flexed to an angle of 60°, and the knee flexed to an angle of 60° to 90°. While stabilizing the hip, the examiner internally rotates and adducts the hip by applying downward pressure to the knee (Fig. 7.11).

Investigations

Most cases of acute low back pain irrespective of the cause subside within 4–6 weeks. Hence no radiological imaging is warranted during this period, the exception being presence of red flags. In case the patient presents with any of the red flags mentioned above, magnetic resonance imaging of the lumbosacral spine is indicated. A plain X-ray of the lumbosacral spine is more than sufficient during the initial management of acute low back pain.[14]

Blood Tests

Complete hemogram with inflammatory markers like ESR, CRP, platelets, RA factor, HLA B 27, uric acid levels is must when infective or inflammatory back pain is suspected.

Radiology

X-ray can reveal minor to major fractures of the spine, spondylolisthesis which can be the cause of the patient's low back pain. MRI of the lumbosacral spine is indicated when there is a red flag during initial evaluation. It helps in identifying serious disorders like tumor, large disc herniations in case of cauda equina syndrome, a spinal hematoma, abscess or infective foci in the spine. Disadvantage is it is more expensive. CT scan—CT shows bony details better than MRI does. Hence, it is preferred when one needs to evaluate bony details (fractures, scoliosis) and when there are contraindications to MRI, as in patients with metal implant devices.

Fig. 7.11: FAIR test

Electrodiagnostic Studies

Nerve conduction studies (NCV) and electromyographs (EMG) may be used in patients with radiculopathy when clinical examination suggests multilevel root lesions, when symptoms do not match imaging studies, and when patients have breakaway weakness.

Biopsy and Culture

In cases of osteomyelitis and for histopathologic diagnosis of infection, malignancy, or other lesions.

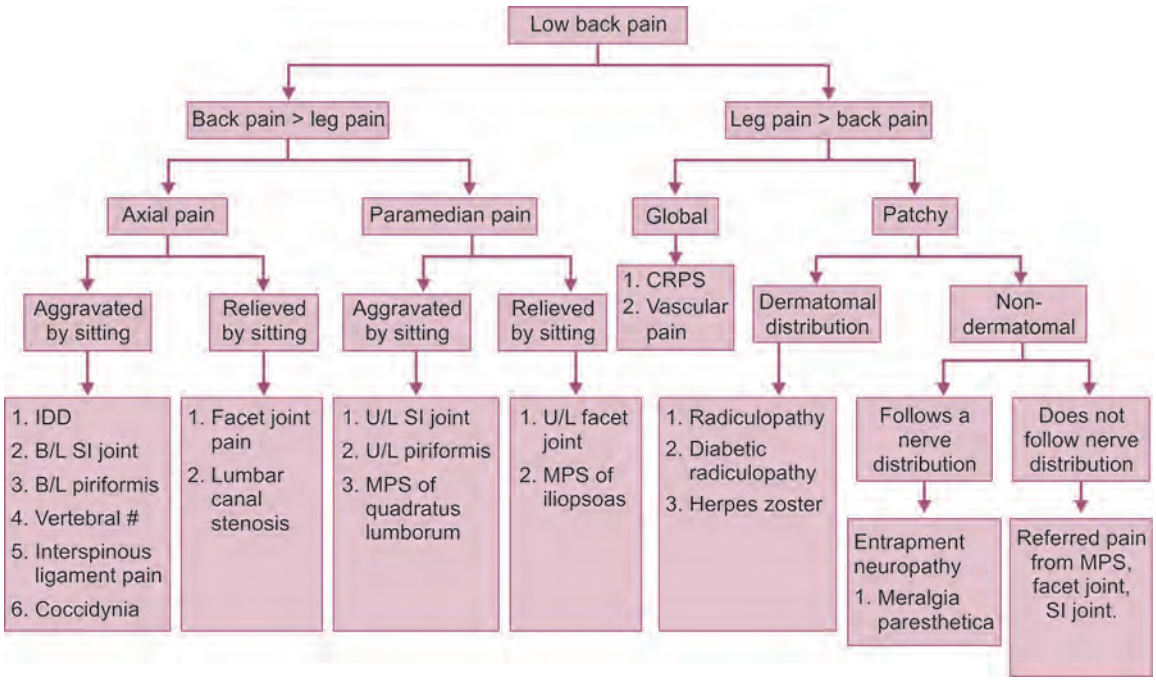
LOW BACK PAIN ALGORITHM

Case example—A 48 year old male patient presented with lower back pain radiating down the lateral side of right leg and foot up to great toe. It was gradual in onset with intensity of 9 of 10 on NRS. Pain was associated with burning and tingling sensation over the right foot. Back pain was aggravated by sitting, standing and bending forward and leg pain was aggravated on walking with partial relief on lying down and after taking analgesics like oral diclofenac. Past history of trauma, fever, cough and weight loss was not present. Bladder bowel function was normal.

On exam, SLR was positive on right side at 30°.

Sensory loss was present over dorsum of right foot (space between first and second toe) weak dorsiflexion of right foot (foot drop) sluggish plantar reflex.

Tenderness was present on L5–S1 paramedian region.



REFERENCES

1. Mersky H, Bogduk N. (eds). Classification of Chronic Pain: Description of Chronic Pain Syndromes and Definition of Pain Terms. 2nd edition. Seattle: IASP press; 1994.
2. van Tulder M, Becker A, Bekkering T, Breen A, del Real MTG, Hutchinson A, et al. European guidelines for the management of acute nonspecific low back pain in primary care. Eur Spine J (2006) 15 (Suppl. 2): S169–91.
3. Fishman SM, Ballantyne JC, Rathmell JP. Bonica's Management of Pain, 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
4. van Kleef M, Vanelderen P, Cohen SP, Arno Lataster A, Van Zundert J, Mekhail N. Pain Originating from the Lumbar Facet Joints. Pain Practice. 2010; 10(5): 459–69.
5. Vanelderen P, MD, Szadek K, Cohen SP, De Witte J, Lataster A, Patijn J, Mekhail N, van Kleef M, Van Zundert J. Sacroiliac Joint Pain. Pain Practice. 2010;10(5): 470–8.
6. Discogenic Low Back Pain.Kallewaard JW, Terheggen MABM, Groen GJ, SluijterME, Derby R, Kapural L, Mekhail N, van Kleef M, Pain Practice. 2010; 10(6): 560–79.
7. Boxem KV, Cheng J, Patijn J, van Kleef M, Lataster A, Mekhail N, Van Zundert J. Lumbosacral Radicular Pain. Pain Practice. 2010; 10(4): 339–58.
8. Patijn J, Mekhail N, HayekS,Lataster A, van Kleef M, Van Zundert J. Meralgia Paresthetica. Pain Practice. 2011; 11(3): 302–8.
9. Das G, Mehta P, Roy C. How to start and run a pain clinic. New delhi:Wiley;2013.
10. Hawker GA, Mian S, Kendzerska T, French M. Measures of Adult Pain. Arthritis Care & Research. 2011Nov; 63(11): S240–S252.
11. Eisenstein SM, Parry CR. The lumbar facet arthrosis syndrome. The journal of bone and joint surgery.1987 Jan; 69-B (1): 3–9.
12. Patijn J, Janssen M, Hayek S, Mekhail N, Van Zundert J, van Kleef M. Coccygodynia. Pain Practice, Volume 10, Issue 6, 2010 554–9.
13. Lirette LS, Chaiban G, Tolba R, Eissa H. Coccydynia: An Overview of the Anatomy, Etiology, and Treatment of Coccyx Pain. The Ochsner Journal. 2014; 14:84–87.
14. Das G. Clinical methods in pain medicine. New Delhi: CBS Publishers & Distributors; 2015.

CHAPTER

8

Management of Back Pain

Rammurthy

As discussed previously, most of the acute low back pain patients recover within 4–6 weeks; invasive treatment is not indicated unless there are red flags. So the main treatment is conservative, aimed at symptom control and patient education.

I. CONSERVATIVE MANAGEMENT

A. Pharmacological Management

The choice of analgesic depends on the type of pain and underlying etiology.

If the pain is nociceptive in nature (aching, pressing, no tingling or burning) as in case of facet joint pain, sacroiliac joint pain, myofascial pain, ligament sprain:

1. Non-steroidal anti-inflammatory drugs (NSAIDs) are highly effective in acute low back pain but are limited by their serious adverse effects. Hence NSAIDs should be restricted to only a short duration (5–7 days).
2. Simple analgesic like paracetamol at the dose up to 3 g/day can be started and the dose reduced after 10 days. Although less effective than NSAIDS, it has less adverse effects and is safe since they are less effective, they should never be prescribed as monotherapy. They are useful in mild to moderate pain.
3. Opioids—weak opioids like tramadol can be given in acute low back pain both as monotherapy and in combination with NSAIDs and paracetamol.

If the pain has neuropathic component (tingling, numbness, burning, shooting, electric shock like) as in case of acute radicular pain, acute herpes zoster, entrapment neuropathies, then it is wise to start anti-neuropathic drugs.

1. Pregabalin started with 75 mg once or twice a day and dose gradually increased depending on the patient tolerance.
2. Gabapentin started with 100 mg thrice a day and the dose is gradually increased. Maximum dose is 3600 mg/day.

Both of these drugs are used in case of pain which is sharp, shooting as in radiculopathy or entrapment neuropathy:

Pain which is of burning quality better responds to antidepressants like:

1. Amitriptyline 5–10 mg and increased up to a maximum dose of 100 mg per day.
2. Nortriptyline 5–10 mg per day (Table 8.1).

B. Psychological Interventions

Chronic pain is associated with psychological disturbances and hence need proper counseling and treatment of associated depression, anxiety.

C. Non-pharmacological Treatment

A. Back Pain More than Leg Pain

Causes may be disc degeneration, facet joint arthropathy, myofascial pain, sacroiliac joint arthopathy or multifactorial.

Table 8.1: 2010 International Association for the Study of Pain (IASP) prescribing recommendations for first-line medications

Medication	*Starting dose*	*Titration*	*Max. dosage*	*Trial duration*
$\alpha_2\delta$ ligands				
Gabapentin	100–300 mg at bedtime or tid	↑ by 100–300 mg tid every 1–7 days	3600 mg/day	3–8 weeks + 2 weeks at max. dose
Pregabalin	50 mg tid or 75 mg bid	↑ to 300 mg/day after 3–7 days, then by 150 mg/day every 3–7 days	600 mg/day	4 weeks
SNRIs				
Duloxetine	30 mg qd	↑ to 60 mg qd after 1 week	60 mg bid	4 weeks
Venlafaxine	37.5 mg qd	↑ by 75 mg each week	225 mg/day	4–6 weeks
TCAs Desipramine nortriptyline	25 mg at bedtime	↑ by 25 mg/day	150 mg/day	6–8 weeks, with ≥ 2 weeks at max. tolerated dosage
Topical lidocaine	Max. 3.5% patches/ day for 12 h max.	None needed	Max. 3 patches/day for 12–18 h max.	3 weeks

SNRIs = serotonin-norepinephrine reuptake inhibitors, TCAs = tricyclic antidepressants
Dworkin RH, et al. Maya Clin Prac 2010; 85 (3 Suppl): S314.

1. Reassurance and patient education.
2. Back school: A term generally used for group classes that provide education about back pain. They generally include information about anatomy and function of the spine, common sources of low back pain, proper lifting technique, ergonomic techniques, advice about exercise and remaining active.[1]
3. Exercise: Strengthening and flexibility exercises and correction of deficits in kinetic chain.[2]
4. Specific exercise treatment for low back pain—postural retraining, stretching tight areas, strengthening weak areas, lumbar stabilization, obtaining and maintaining mild abdominal contraction and multifidus activation, strengthening of quadratus lumborum by side bridging, extensor strengthening in quadruped and pelvic floor exercises, breathing exercises. Modifications for those in whom exercises aggravate pain in the form of curl ups instead of sit ups and leg raises in quadruped position with leg extended instead of lying prone and extending the spine and arms and legs.
5. Flexion exercises for low back pain: Partial sit ups, single knee to chest, double knee to chest, hip flexor stretching, full squats (Williams).[3]
6. Extension exercises for low back pain–Prone lying with cervical rotation to right and left, prone on elbows, progressive extension on pillows, prone on hands, standing extension (McKenzie).[4]
7. Aerobic activity: Faster walking with swinging of arms.[5]
8. Aquatic exercises: Patients can learn neutral position, stabilizing and other strengthening exercise, and by walking, jogging (these can be done in deep water using a buoyancy belt or vest) or swimming can add an aerobic component.[6]
9. Exercise after spine surgery is effective to decrease pain and return to work.[7]

10. Manual mobilization or manipulation: These are designed to apply pressure and shearing forces to the layers of fascia, separating them, resulting in restoration of fluidity, nutrition, elasticity and freedom of movement. Temporary relief may occur from mechanoreceptor stimulation, stretch of adhesions or restoration of shortened muscle length. Patients own isometric contractions can aid in mobilization and make them less painful.[8]
11. Traction: Multiple randomized controlled trials using different doses of traction have found traction to be ineffective for treatment of back pain.[10,11]
12. Heel lifts and correction of leg length discrepancy. Small unblended studies have found that correction of leg length discrepancy decreases low back pain but this has not been evaluated in large controlled trials.[13]
13. Lumbar supports: There is no consistent evidence that lumbar supports prevent the occurrence of back pain.[14]
14. Transcutaneous electric nerve stimulation is helpful for temporary relief of pain.
15. Massage: It is helpful in different conditions. There are four basic strokes of massage:
    a. Efflurage—used for lymphatic drainage, joint sprains, muscle strains, CRPS.
    b. Petrissage—used to promote relaxation and increased blood flow.
    c. Friction massage—used for tendonitis, bursitis, trigger points.
    d. Tapotement—used to loosen secretions over sinuses.[15]
16. Complimentary movement therapies:
    a. Yoga—promotes relaxation by mind body therapy, stretching and breathing exercise.
    b. Pilates—a form of core strengthening exercise.
    c. Alexander technique—corrects the posture and movement patterns.[16]
    d. Feldenkrains—a combination of classes and hands on work with therapeutic exercise.[17]
17. Physical therapy for gait training, core stability, lower extremity biomechanics. Occupational therapy for proper posture and ergonomics. Relaxation training for meditation and hypnosis.

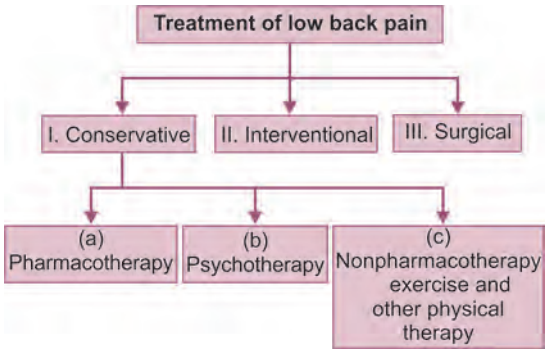


Fig. 8.1: Algorithm for management of low back pain

b. Leg Pain More Than Back Pain

1. Lumbosacral radiculopathy: Relative rest for 1–3 days followed by gradual exercise program based on the site of disc herniations
2. Lumbar spinal stenosis:
    a. Flexion based lumbar stabilization exercises strengthening of abdominals, pelvic girdle stabilizes and gluteals
    b. Stretching of iliopsoas and rectus femoris
    c. Aerobic conditioning
    d. Bracing with abdominal corset for overweight patients with protuberant abdomen
3. Non-lumbar spine causes of radicular leg symptoms:
    a. Joint disorders:
        i. Sacroiliac joint–mobilizing exercises
        ii. Hip joint—range of motion and isometric strengthening exercises
    b. Soft tissue disorders:
        i. Piriformis syndrome—piriformis stretching exercises

ii. Greater trochanteric pain syndrome—neuromuscular re-education of gluteal muscles and strengthening exercises
iii. Iliotibial band syndrome—iliotibial band stretching and strengthening exercses
iv. Myofascial pain syndromes—trigger point injections by dry needling and/or local anesthetic and steroid injections

II. INTERVENTIONAL PAIN MANAGEMENT

When the low back pain persists for more than 6 weeks with or without treatment and pain is more than mild, poorly responds to treatment with drugs and hence require multimodal approach to manage chronic low back pain where interventional techniques are required. A few simple interventions like trigger point injections can be even done by primary care physicians.

a. Facet Joint Pain

C-arm/USG/CT guided intra-articular facet joint block or medial branch blocks are definitive diagnostic for facet joint arthropathy and are usually followed by steroid injection or radiofrequency ablation of medial branches for long term results. Cooled radiofrequency and cryoneurolysis are other procedures for ablation of medial branches with good results.

b. Sacroiliac Joint Pain

Diagnosis of sacroiliac joint pain are also confirmed by diagnostic local anesthetic injection into the joint when more than 50% of pain is relieved. Long-term pain relief may be by cooled radiofrequency or cryoneurolysis of lateral branches supplying sacroiliac joint. Intra and periarticular injection may provide short term relief.

c. Discogenic Pain

Short-term relief is possible with caudal epidural steroid injection. For long-term relief there are many interventions, but only biacuplasty has the best evidence. IDET, intradiscal methylene blue, PRP, rami communicates block has been tried with various responses.

d. Radicular Pain due to Prolapsed Intervertebral Disc

Interventions range from transforaminal epidural steroid injections, percutaneous discectomies, percutaneous nucleolysis by ozone, laser, to endoscopic discectomy.

e. CRPS and Vascular Pain

Lumbar sympathetic block is useful where the pain is sympathetically maintained. In extreme cases, spinal cord stimulation may be required to control the pain.

f. Myofascial Pain and Trigger Point Injections

Trigger point injection is the usual treatment for the myofascial pain and can be done in the outpatient set up by the physician. Dry needling with solid filament or local anesthetic or botox injection in to the trigger points is carried out.

III. SURGICAL MANAGEMENT

It is a general rule that presence of red flags warrants surgical management in most situations. Failure of conservative management and interventional management may also need surgical management if pain is moderate to severe.

REFERENCES

1. Deyo RAR, Kent D. What can the history and physical examination tell us about back pain. JAMA 1992;268960:760–5.
2. van Tulder MW, Esmail R, Bombardier C, et al. Back schools for nonspecific low back pain. Cochrane database Syst Rev 2000;2:CD000261.

3. Hodges PW. Core stability exercise in chronic low back pain. Orthop Clin North Am.2003:34(2) 245–54.
4. Blackburn SE, Portney LG. Electromyographic activity of back musculature during Williams flexion exercises. Phys Ther.1981;61: 875–85.
5. Fiebert I, Keller CD. Are "passive" extension exercises really passive? J Orthop Sports Phys Ther 1994 Feb; 19(2): 111–6.
6. Mc Gill S. Normal and injury mechanics of the lumbar spine. In:Low back disorders: evidence based prevention and rehabilitation. Champaign: Human Kinetics;2002:87–136.
7. Konlian C. Aquatic therapy: making a wave in the treatment of low back pain.Orthop Nurs 1999;18 (1):11–20.
8. Ostelo RW, de Vet HC, Wadell G, et al. Rehabilitation following first time lumbar disc surgery; a systematic review within the framework of the Cochrane Collabration. Spine 2003; 28(3): 209–18.
9. Nelemans PJ, de Bie RA, de Vet HCW, et al. Injection therapy for subacute and chronic benign low – back pain (Cochrane review). Cochrane Database Syst Rev.2000; 2:CD001824.
10. Greenman PE. Principles of manual medicines. Baltimore: Williams and Wilkins.1989.
11. Van Tulder MW, Goossens M, Waddell G, et al. Conservative treatment of chronic low back pain. In NachemsonAl (eds). Neck and back pain: the scientific evidence of causes, diagnosis and treatment. Philadelphia: Lippincott Williams and wilkins; 2000:271–304.
12. Van Tulder MW, Waddell G. Conservative treatment of acute and subacute low back pain. In: Nachemson AL, Jonsson E, eds. Neck and back pain: the scientific evidence of causes, diagnosis and treatment. Philadelphia: Lippincott Williams and Wilkins; 2000: 241–69.
13. Brady RJ, Dean JB, Skinner TM, et al. Limb length inequality:clinical implications for assessment and intervention. J Orthop Sports Phys Ther 2003; 33(5): 221–34.
14. Van Tulder MW, Jellema sP, van Poppel MN, et al. Lumbar supports for prevention and treatment of low back pain (Cochrane reviw). Cochrane database Syst Rev 2000;3:CD001823
15. Furlan AD, Brosseau L, Imamura M, et al. Massage for low back pain Cochrane Database Syst Rev 2002;2: CD001929.
16. Ernst E, (ed). The desktop guide to complimentary and alternative medicine. 1st ed. London: Mosby; 2001.
17. Lundblad I, Elert J Gerdle B. Randomized control trial of physical therapy and Feldenkrais interventions in female workers with neck shoulder complaints. J Occup Rehabil 1999;9:179–94.

CHAPTER

9

Myths Related to Low Back Pain

Rammurthy

There are many misconception (myths) regarding low back pain not only among the general population but also among the treating physicians.[1,2] Low level of education among the population is considered as an important factor for the prevalence of these myths.[2] These myths are also difficult to remove or eradicate from the minds of the people or treating physicians. Not surprisingly myths about low back pain and its management are also highly prevalent in Indian subcontinent.[3] These myths are obstacles in the management of the low back pain. Understanding and accepting the facts help in the proper management of the low back pain.

1. **MRI of the lumbosacral spine is a must whenever there is a patient of acute low back pain in the clinic.**

   Fact—MRI of the lumbosacral spine is not indicated in acute low back pain in the absence of red flags. 70–90% of patients recover from acute low back pain within 2–4 weeks of onset with conservative therapy in the absence of red flags.[4,5] There is a poor correlation between the low back pain and the MRI findings.[6] Patients with severe degenerative changes in the spine may not have any pain. Similarly abnormal findings are also frequently seen in MRI of asymptomatic individuals.[7,8] Immediate imaging in case of acute low back pain without any serious underlying cause (red flags) is of no help and does not improve the overall outcome. It is associated with radiation exposure, increased treatment costs and may lead to unnecessary procedures.[9] Hence physicians should refrain from advising MRI of the spine in case of acute low back pain if there are no red flags.[10]

2. **Spondylosis is the most common cause of the low back pain.**

   Fact—spondylosis is not the cause of low back pain.

   Sponylosis is not a clinical but radiologic terminology, and it merely indicates degenerative change in any part of the spine. It does not constitute a specific diagnosis. The most common cause of low back pain in elderly age group is facet joint arthropathy due to degenerative osteoarthritis[11], followed by sacroiliac joint arthropathy (again degenerative).[12] The common cause of low back pain in middle or younger age group is internal disc disruption.[13] Spondylosis is a nonspecific term and hence its use in the clinical setting should be discouraged.

3. **Complete bed rest, restriction of bending or extreme movements and lying down on a hard surface is helpful and is indicated until the patient is fully recovered from the pain.**

   Fact—prolonged bed rest and restriction of movements is not indicated.

   Again this is a commonest myth among many treating physicians and neurosur-

geons and spine surgeons. As previously thought prolonged bedrest is not required and early return to work and staying active is encouraged.[14,15] Bedrest is contraindicated according to some guidelines.[16] Bedrest is indicated only for short duration (1–2 days) and patient is encouraged to stay active. Prolonged bedrest may cause muscle wasting due to disuse atrophy and thus may actually be harmful.

4. **Lumbosacral belt or brace helps in reducing the pain.**

   Fact—lumbosacral belts or braces are no more recommended.

   This is also a common practice among many orthopedic spine surgeons and neurosurgeons. More than 99% of orthopedic surgeons in USA admitted that they prescribe lumbosacral braces for low back pain.[17] Lumbosacral braces or belts have not shown to improve the prognosis of the low back pain.[18] Use of the braces may lead to lumbar muscle deconditioning and weakness of the paraspinal muscles. Paraspinal muscles are the important muscles supporting the spine and wasting of these muscles can do more harm than the benefit.

5. **Surgery is indicated whenever there is disc bulge or prolapse/any other abnormality in the MRI of patient with back pain.**

   Fact—surgery is indicated only when there are red flags.

   This is a common myth among the treating physicians and the patients that the MRI/X-ray of the back (lumbosacral spine) will reveal the cause of the back pain. Most of the surgeons make a decision to go ahead with spine surgery just based on the radiologic findings. In one of the studies, >50% of the patients agreed to undergo spine surgery just based on the MRI findings without any symptoms.[19] More than 40% of patients did so based on the findings on plain radiographs. About 33% patients believed that surgical treatment was more effective than nonsurgical treatment and some patients thought that spine injections were riskier than surgery. The benefits of spinal fusion surgeries for the treatment of back pain are limited with worst outcomes. In the US, increase in the number of surgeries with the introduction of new implants was associated with more complications. They did not improve pain.[20] And not all the radiculopathies (sciatica) associated with disc prolapse are the indications for surgery. Minimally invasive percutaneous procedures like lumbar transforaminal, lumbar interlaminar, caudal epidural steroid injections have shown to be effective in treating chronic low back pain.[21] Surgery in indicated only in the presence of neurologic deficits or other serious disorders like tumors, infections (red flags).

6. **Always sit up straight to avoid back pain.**

   Fact—sitting up too straight and still for long periods can also be a strain on your back.

   Fact—slouching is bad—but sitting straight without changing the posture for longer duration of time is also bad for the lumbar spine. instead frequent change of posture from sitting to standing every 30 minutes helps in reducing strain on the lumbar spine and hence back pain.

7. **Calcium supplements will help in treating low back pain.**

   Fact—calcium supplements may not benefit in low back pain.

   Studies have shown that vitamin D levels are normal in patients with low back pain. Hence calcium and Vitamin D supplements are of little help in patients with low back pain.

REFERENCES

1. Ihlebaek C, Eriksen HR. Myths and perceptions of back pain in the Norwegian population, before and after the introduction of guidelines for acute back pain. Scand J Public Health. 2005; 33(5): 401-6.
2. Ihlebaek C, Eriksen HR. The "myths" of low back pain: status quo in Norwegian general practitioners and physiotherapists. Spine (Phila Pa 1976). 2004 Aug 15; 29(16):1818–22.
3. Pagare VK, Dhanraj T, Thakkar D, Sareen A, Palekar TJ. Beliefs about low back pain: Status quo in Indian general population. J Back Musculoskelet Rehabil. 2014 Dec 10. [Epub ahead of print]
4. Coste J, Delecoeuillerie G, Cohen de Lara A, Le Parc JM, Paolaggi JB. Clinical course and prognostic factors in acute low back pain: an inception cohort study in primary care practice**.** BMJ 1994; 308:577–80**.**
5. Grotle M, Brox JI, Veierød MB, Glomsrød B, Lønn JH, Vøllestad NK. Clinical course and prognostic factors in acutelow back pain: patients consulting primary care for the first time. Spine (Phila Pa 1976). 2005 Apr 15; 30(8):976–82.
6. Maataoui A, Vogl TJ, Khan MF. Magnetic resonance imaging-based interpretation of degenerative changes in the lower lumbar segments and therapeutic consequences. World J Radiol. 2015 Aug 28; 7(8): 194–7.
7. Deyo RA, Mirza SK, Turner JA, Martin BI. Overtreating Chronic Back Pain: Time to Back Off? J Am Board Fam Med. 2009; 22(1): 62–8.
8. Willems P. Decision making in surgical treatment of chronic low back pain: the performance of prognostic tests to select patients for lumbar spinal fusion. Acta Orthop Suppl. 2013 Feb; 84(349):1-35.
9. Andersen JC. Is Immediate Imaging Important in Managing Low Back Pain? Journal of Athletic Training 2011; 46(1):99–102.
10. Chou R, Fu R, Carrino JA, Deyo RA. Imagingstrategies for low-back pain: systematic review and meta-analysis. Lancet. 2009 Feb 7; 373 (9662):463–72.
11. van Kleef M, Vanelderen P, Cohen SP, Arno Lataster A, Van Zundert J, Mekhail N. Pain Originating from the Lumbar Facet Joints. Pain Practice. 2010; 10(5): 459–69.
12. Vanelderen P, MD, Szadek K, Cohen SP, De Witte J, Lataster A, Patijn J, Mekhail N, van Kleef M, Van Zundert J. Sacroiliac Joint Pain. Pain Practice. 2010; 10(5): 470–478.
13. Discogenic Low Back Pain. Kallewaard JW, Terheggen MABM, Groen GJ, Sluijter ME, Derby R, Kapural L, Mekhail N, van Kleef M, Pain Practice. 2010; 10(6): 560–79.
14. van Tulder M, Becker A, Bekkering T, Breen A, del Real MTG, Hutchinson A, et al. European guide-lines for the management of acute nonspecific low back pain in primary care. Eur Spine J (2006) 15 (Suppl. 2): S169–S191.
15. Casazza BA. Diagnosis and Treatment of Acute Low Back Pain. Am Fam Physician. 2012; 85(4):343–50.
16. Koes BW, van Tulder M, Lin CWC, Macedo LG McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J (2010) 19:2075–94.
17. Saunders HD. Regarding the controversy of lumbosacral supports and braces—an update. J Back Musculoskelet Rehabil. 1993 Jan 1; 3(3):21—30.
18. van Duijvenbode IC, Jellema P, van Poppel MN, van Tulder MW. Lumbar supports for prevention and treatment of low back pain. Cochrane Database Syst Rev. 2008 Apr 16; (2):CD001823.
19. Franz EW, Bentley JN, Yee PP, Chang KW, Kendall-Thomas J, Park P, Yang LJ. Patient misconceptions concerning lumbarspondylosis diagnosis and treatment. J Neurosurg Spine. 2015 May; 22(5): 496–502.
20. Cahana A, Mavrocordatos P, Geurts JW, Groen GJ.Do minimally invasive procedures have a place in the treatment of chronic low back pain? Expert Rev Neurother. 2004 May; 4(3):479–90.
21. Benyamin RM, Manchikanti L, Parr AT, Diwan S, Singh V, Falco FJ, Datta S, Abdi S, Hirsch JA. The effectiveness of lumbar interlaminar epidural injections in managing chronic low back and lower extremity pain. Pain Physician. 2012 Jul-Aug; 15(4):E363–404.
22. Thorp AA, Kingwell BA, Owen N, Dunstan DW. Breaking up workplace sitting time with intermittent standing bouts improves fatigue and musculoskeletal discomfort in overweight/obese office workers. Occup Environ Med. 2014 Nov;71 (11):765–71.
23. Thörneby A, Nordeman LM, Johanson EH. No association between level of vitamin D and chronic low back pain in Swedish primary care: a cross-sectional case-control study. Scand J Prim Health Care. 2016 Jun;34(2):196–204.

III

SECTION

III

Neck Pain Management

Ravi Shankar Sharma, Sunita Lawange and Pankaj Surange (Section Editors)

10. Pain Generators of Neck
11. Examination of Patients with Neck Pain
12. Management of Neck Pain
13. Myths in Neck Pain

CHAPTER

10

Pain Generators of Neck

Rammurthy and Ravi Shankar Sharma

Neck pain is the second most common type of spine pain after low back pain. The Bone and Joint Decade 2000–2010 Task Force on neck Pain and its associated disorders defines neck pain as pain located in the anatomical region of the neck with or without radiation to head, trunk, and upper limbs.[1] Several structures in the cervical spine can be the source of pain. Hence, it is important to understand the anatomy of these structures which can aid in diagnosing painful conditions of the neck.

CERVICAL VERTEBRAE

The cervical spine has seven vertebrae out of which three are atypical and four are typical vertebrae. The cervical spine is convex anteriorly. The typical vertebrae are from C3-6, which have similar anatomical characteristics.[2] The atypical vertebrae are C1, C2 and C7, which have unique characteristics that makes them different from each other and also from the typical vertebrae (Fig. 10.1).

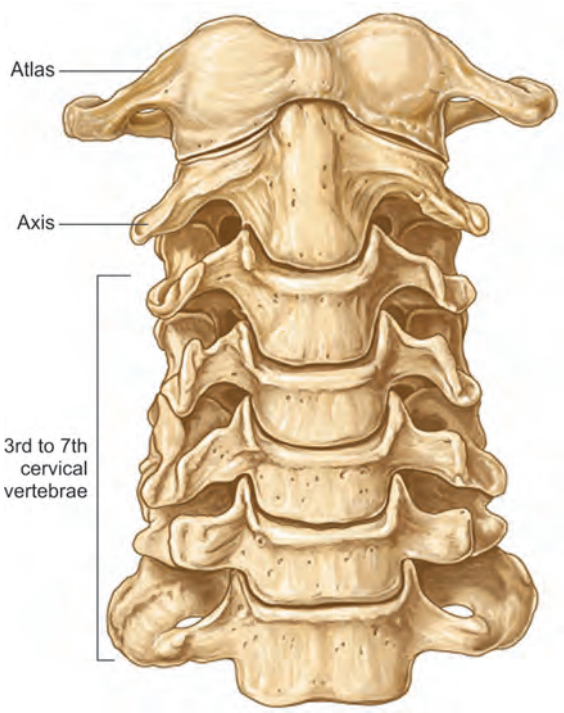


Fig. 10.1: Cervical spine

1. Typical Cervical Vertebra

A typical cervical vertebra has a body which is proportionately small compared to posterior elements and is almost circular in shape. The body is concave on its upper surface and convex on its lower surface in the transverse plane. The anteroinferior margin of one vertebra projects over the anterosuperior border of the lower vertebra immediately below. The upper surface of each vertebra projects two processes laterally on either side, which are called the uncinate processes. They articulate with the lower notches of the upper vertebra to form the uncovertebral joints or joints of Luschka.[3] Posteriorly, two pedicles project on either side which leads to the articular pillar with superior and inferior articular surfaces. The inferior articular surface of the one vertebra articulates with the superior articular surface

of the next lower vertebra to form facet joint. The plane of the facet joints are placed almost horizontally so that the superior articular surface faces upwards and slightly backwards and inferior articular surface faces downwards and forwards.

Laterally, projected are the two transverse processes which have anterior and posterior tubercles and a foramen called foramen transversarium. The anterior tubercle of the transverse process of the C6 vertebra is called the Chassaignac's tubercle which is an important land mark for the stellate ganglion block. Cervical spinal nerve root exits between the two tubercles of the transverse process of the corresponding vertebra. The vertebral artery and vein along with the sympathetic plexus of nerves passes through the foramen transversarium.

The laminae are short and are fused at the origin of spinous process. The spinous process of the typical cervical vertebra projects posteriorly and slightly inferiorly and is bifid.

2. Atypical Cervical Vertebra

a. Atlas (C1 Vertebra) (Fig. 10.2)

The first cervical vertebra does not have a body and is ring shaped. It is also devoid of the spinous process.[3] Thus the atlas has anterior and posterior arches and two lateral masses.[4] The posterior surface of the anterior arch makes articulation with the dens (odontoid process) of the C2 vertebra to form atlantoaxial joint which allows lateral rotation of the neck.[5] The lateral masses have the articular processes and transverse processes. The superior articular processes make articulation with the occipital condyles to form atlanto-occipital joint. This joint allows flexion and extension movements of the neck.[5] The transverse processes have foramen transversarium for the vertebral artery and vein.

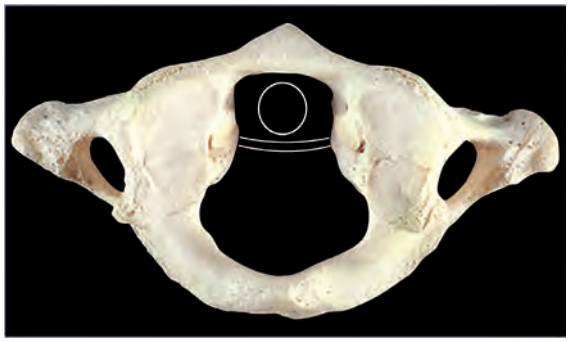


Fig. 10.2: C1 vertebra or the atlas

b. Axis (C2 Vertebra) (Fig. 10.3)

The important function of the second cervical vertebra is to bear the load of the head and atlas and also to transmit the load to the remainder of the cervical spine.[5] Second cervical vertebra (axis) has an odontoid process (dens) which is fused with the body and is directed superiorly to make an articulation with the anterior arch of atlas.[3] This joint allows lateral rotation movements. Contrary to atlas, axis has a short spinous process. The transverse processes of axis also have foramen transversarium to allow vertebral artery and vein.

c. C7 Vertebra (Fig. 10.4)

The seventh cervical vertebra is distinguished by its long, non-bifid and prominent spinous process called the vertebra prominens. Although the transverse processes have

Fig. 10.3: C2 vertebra or the axis

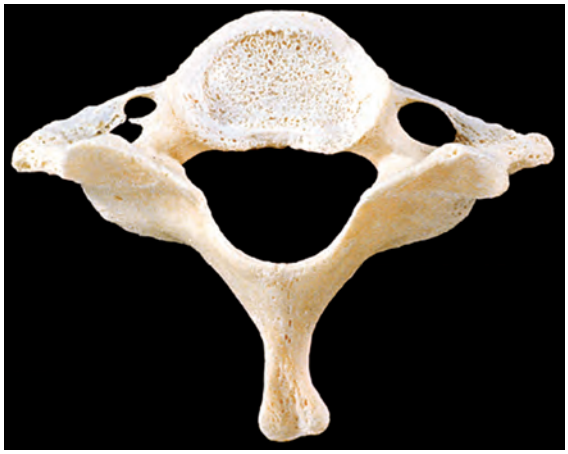


Fig. 10.4: C7 vertebra

foramen transversarium, they only allow the accessory vertebral vein to pass through it.

The cervical vertebrae also are supported by numerous ligaments just like in the lumbar region such as anterior and posterior longitudinal ligaments, interspinous, supraspinous ligaments and ligamentum flavum. The cervical spine is also supported by numerous muscles like flexors (scalene, longus colli, longus capitis), extensors (trapezius, levator scapulae, splenius cervicis, splenius capitis, and iliocostalis), and sternocleidomastoid muscles.

INTERVERTEBRAL DISCS[3]

Intervertebral disc is absent between C1 and C2 vertebrae and is present at all other levels. The disc has annulus fibrosus, nucleus pulposus and end plates. There are some differences between cervical and lumbar intervertebral discs. The cervical discs are much contained within the vertebral bodies than in the lumbar area due to the concavity on the upper surface. The annulus is also much thicker posteriorly than in the lumbar region. The nucleus pulposus is located more anteriorly within the disc as compared to the lumbar discs and disappears early in life than their lumbar counterparts. Hence cervical disc prolapse is uncommon after the age of thirty.

THE VERTEBRAL CANAL, INTERVERTEBRAL FORAMEN AND THE NEURAL STRUCTURES (SPINAL CANAL) (Figs 10.5 and 10.6)

Image of Cervical Vertebrae with Cervical Epidural Space and Structures Traversing the Epidural Space

The spinal canal in the cervical region is formed by vertebral foramina of all the cervical vertebrae. The boundaries of the cervical spinal canal are same as in lumbar spinal canal. The normal anteroposterior spinal canal diameter in cervical region is

Fig. 10.5: Intervertebral foramina of the cervical spine as seen in oblique view

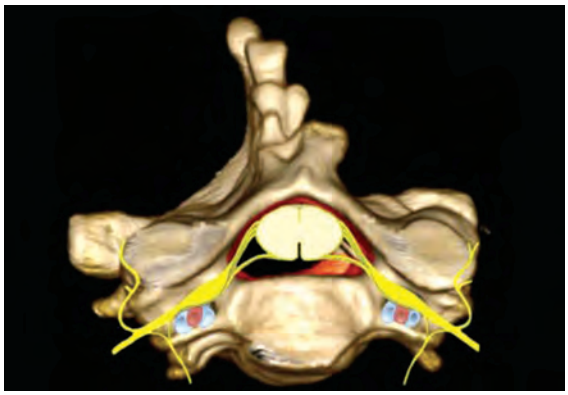


Fig. 10.6: Cervical spinal canal

14 ± 1.5 mm.[6] When the canal diameter is reduced to less than 10 mm, the spinal cord gets compressed leading to quadriparesis or quadriplegia, sensory loss from the level of neck below, bowel and bladder disturbances. This condition is called cervical myelopathy which is a surgical emergency. The spinal cord with its meningeal coverings passes through the spinal canal.

Intervertebral Foramen

Intervertebral foramen is present in between two consecutive pedicles. The boundaries are:

1. Anteriorly, the vertebral body, uncinate process.
2. Posteriorly by facet joints
3. Superiorly and inferiorly by pedicles.

The diameter of the intervertebral foramen is reduced during neck extension and ipsilateral rotation. This can aggravate the symptoms of radiculopathy and is an important sign. Each cervical spinal nerve exits via the intervertebral foramen which is directed anterolaterally and slightly inferiorly. There are eight cervical spinal nerves. Each cervical spinal nerve runs above their respective vertebra except for the C8 nerve which runs above T1 and below the C7 vertebra as there is no eighth cervical vertebra. Further down in thoracic and lumbar region, the spinal nerves run below their respective vertebrae. Each spinal nerve runs over the bifid transverse process behind the vertebral vessels within the intervertebral foramen.

FACET JOINTS

The zygapophyseal or facet joints are true joints with cartilaginous surfaces lined with synovium, containing synovial fluid and surrounded with a ligamentous joint capsule. As such, they are subject to the same inflammatory and degenerative diseases found in other synovial joints. The cervical zygapophyseal joints provide a guiding and gliding movement between the adjacent cervical joint. Each facet joint is formed by the articulation of superior articular process of one vertebra and inferior articular process of the immediate upper vertebra. Facet joints are supplied by medial branch of the dorsal rami of the spinal nerve of that level and also the medial branch from the immediate upper spinal nerve.

Conclusion

The unique anatomy of cervical spine and upper extremity balances the attributes of strength and stability with those of flexibility and range of motion.

REFERENCES

1. Guzman J, Hurwitz EL, Carroll LJ, Haldeman S, Côté P, Carragee EJ, Peloso PM, van der Velde G, Holm LW, Hogg-Johnson S, Nordin M, Cassidy JD, Bone and Joint Decade 20002010 Task Force on Neck Pain and Its Associated Disorders A new conceptual model of neck pain: linking onset, course, and care: the Bone and Joint Decade 20002010 Task Force on Neck Pain and Its Associated Disorders. Spine. 2008;33(4) Suppl.:S14–S23. doi: 10.1097/BRS.0b013e3181643efb. [PubMed] [CrossRef]
2. Sangari SK, Dossous PM, Heineman T, Mtui EP. Dimensions and Anatomical Variants of the Foramen Transversarium of Typical Cervical Vertebrae. Anatomy Research International. Volume 2015, Article ID 391823.
3. Ombregt L. A System of Orthopaedic Medicine. 4th ed. Edinburgh: Churchill Livingstone Elsevier; 2013.
4. Ebraheim NA, Xu R, Nadim Y. The Essential Bony Anatomy of the Cervical Spine Relative to Instrumentation. Pan Arab J Orth Traum. 2; 1:75–82.
5. Mercer SR, Bogduk N. Joints of the Cervical Vertebral Column. J Orthop Sports Phys Ther. 2001; 31(4):174–82.
6. Morishita Y, Naito M, Hymanson H, Miyazaki M, Wu G, Wang JC. The relationship between the cervical spinal canal diameter and the pathological changes in the cervical spine. Eur Spine J (2009) 18:877–83.

CHAPTER

11

Examination of Patients with Neck Pain

Rammurthy and Ravi Shankar Sharma

DEFINITION

IASP has defined cervical spinal pain or neck pain as "pain perceived anywhere in posterior region of cervical spine from superior nuchal line to first thoracic spinous process".

Chronic neck pain can be defined as widespread sensation and hyperalgesia in the skin, muscles, and ligaments on palpation in both active and passive movements in neck and shoulder region.

INTRODUCTION

Neck pain is one of the most common complaint and hence is a major health issue which can have a negative impact on economy. It is more common in adult population with an incidence of 15% in males and 25% in females in age group of 21 to 55 years. The initial evaluation should be comprehensive in order to ascertain not only the etiology of physical symptomatology, but also the impact the patient's disability has on their psychosocial environment.[1]

RED FLAGS

Though chronic neck pain is commonly due to myofascial pain syndrome or facet joint arthropathy, red flags must be rule out. As cervical canal is almost completely occupied by spinal cord, minor reduction in canal diameter will lead to cervical myelopathy, hence careful assessment is important to identify early signs of myelopathy. Occasionaly patients develop high spinal cord compression leading to quadriparesis, respiratory insufficiency, and death.[2] Table 11.1 enlists the red flags in neck pain.

In patients presenting with any of the above signs and symptoms, immediate radiologic assessment has to be done (MRI of the cervical spine) and they should be referred to the neurosurgeon for further management.

Table 11.1: Red flags in case of neck pain

1. History of trauma—Fracture leading to unstable spine, cord compression, myelopathy, vertebral body fracture.
2. Fever, malaise, nuchal rigidity—Meningitis, epidural abscess.
3. Sudden weight loss, anorexia, night pain—Cervical tumors, metastatic lesions, SOL leading to cord compression, vertebral compression fractures.
4. Progressive disturbance of gait, progressive motor or sensory deficits, bladder bowel incontinence—Cervical myelopathy.
5. Acute progressive neurologic and cognitive deficits accompanied by hemodynamic instability dissecting vertebral artery aneurysms and extracranial carotid artery aneurysms.
6. Associated chest pain, tachycardia, and breathlessness on exertion—ischemic heart disease, cervical angina syndrome.
7. Associated Horner's syndrome—pancoast tumor of the lung.
8. History of rheumatoid arthritis, morning stiffness >30 mins, peripheral joints swelling and arthritis—atlantoaxial dislocation, fibromyalgia.

DETAIL HISTORY OF THE PATIENT

The purpose of thorough history with determination of the location, pattern, and distribution of the patient's pain is to establish an initial differential diagnosis that can subsequently be confirmed or ruled out by physical examination, diagnostic laboratory, radiologic and electrophysiological testing.[1]

1. Age of Onset

In pediatric and adolescent patients, trauma or sports injuries are common causes for neck pain. Congenital defects such as Chiari malformations Type 1, short neck syndromes can also lead to neck pain in these age groups.[1] In middle aged adults inflammatory arthritis such as rheumatoid arthritis, seronegative spondyloarthropathies like ankylosing spondylitis, psoriatic arthritis, and reactive arthritis should be considered in differential diagnosis. Degenerative changes are common in elderly patients.

2. Location of Pain

It helps us to know the underlying pain generator. Pain generators in joints and muscles are usually localized. Nerve root compression pain is dermatomally distributed and pain along the peripheral dermatomal and/or myotomal distribution suggests lesions of the cervical or brachial plexus or their branches. Axial neck pain may be due to internal disc disruption or bilateral facet joint. Paramedial pain suggestive of U/L facet joint and its referred pain, myofascial pain or other neck pathologies. Widespread pain can be seen in fibromyalgia, osteoarthritis, rheumatoid arthritis, SLE, hypothyroidism or somatization in severe depression. Infections and neoplasms can cause axial neck pain through bone destruction with irritation of vertebral body periosteal nerves and altered biomechanics of the facet joints and cervical discs.[3]

3. Spread of Pain

Cervical and brachial referral patterns may be secondary to myofascial trigger points or referred pain from cervical facet joints.[1] Pain commonly is referred from the shoulder, heart, lungs, viscera, or temporomandibular joint to the neck region owing to overlapping nerve distribution. Referred pain to the occiput usually indicates pathologic changes in the upper cervical spine and may radiate down the neck and to the ear.[3] If the face, head, or tongue is involved, the upper three nerve roots of the cervical plexus may be affected. Numbness of the neck, shoulder, arm, forearm, or fingers indicates involvement of C5–T1.[3] The referral area in cervical region is listed in Table 11.2.

4. Duration of Pain

Acute pain due to trauma, infection, disc prolapse with neurodeficit, vascular dissection with hemodynamic instabilities must be aggressively investigated and treated to avoid major complications and death. More gradual or insidious onset is common in progressive degenerative, inflammatory or malignant process.

5. Character of Pain

Pain due to musculoskeletal origin are generally dull, aching, deep, throbbing in nature, whereas neuropathic pain are sharp, shooting, electric shock like with tingling and numbness. Nerve root involvement pain is

Table 11.2: Cervical pain referral pathways[3, 4]

Location of pain	*Source*
Upper posterolateral cervical region	C0–1, C1–2, C2–3
Occipital region	C2–3, C3
Upper posterior cervical region	C2–3, C3–4, C3
Middle posterior cervical region	C3–4, C4–5,C4
Lower posterior cervical region	C4–5,C 5–6, C4, C5
Suprascapular region	C4–5, C5–6,C 4
Superior angle of scapula	C6–7, C6, C7
Midscapular region	C7–T1, C7

dermatomally distributed and described along these areas. Dermatomally, C1 and C2 innervate the occiput region; C3 and C4 supply the nape of the neck; C5 supply the deltoid region; C6 innervate the radial aspect of the forearm, thumb and lateral half of index finger; C7 supplies the medial half of index finger, middle finger and the lateral half of ring finger; C8 is for the ulnar side of the ring finger, little finger, ulnar border of the hand; and T1 supplies the medial border of the foream. T2–T12 provide innervations to the chest and abdomen, with T4 being at the nipple line, T10 at the umbilicus, and T12 at the inguinal ligament.[3] Articular symptoms arise from the facet and vertebral joints causing stiffness and localized pain.[3] Poorly localized, burning pain characters are seen in sympathetically mediated pain. Hyperesthesia, allodynia and burning pain suggests complex regional pain syndrome (CRPS).

6. Progression of Neurodeficits

Any progression of sensory or motor dysfunctions due to nerve root or cord compression must be considered as red flag and treated accordingly. Myelopathy can be due to mass effect from a tumor or infection or instability owing to systemic arthritis or connective tissue disorders, but it is often a result of advanced degenerative changes within the cervical spine and large central PIVD.[3] There can be bladder and bowel disturbances with loss of proprioception due to dorsal column compression leading to gait disturbances.[3] Upper motor neuron type of lesion in lower limb, described as stiffness in lower limbs and lower motor neuron type of lesion in upper limb at the level of compression, described as weakness and looseness in upper limb.

7. Aggravating and Relieving Factors

Pain due to spine involvement will be aggravated during movements. Facet joint pain will be aggravated by neck extension, lateral flexion and lateral rotation. Atlanto-occipital joints arthritis is worsened with provocative neck flexion and extension, whereas atlantoaxial arthritis is worsened with rotation.[3] Discogenic pain will be more in forward flexion. Myofascial pain will be aggravated by muscle stretching and palpating over tender points. Radicular pain will be relieved with arm abducted and externally rotated over head. Chronic inflammatory pain is often worsened after a period of inactivity and improves with exercise. Degenerative arthritis is often exacerbated by exercise and improves with rest.[1]

8. Associated Symptoms

Morning stiffness, polyarthritis, rigidity, skin manifestations are associated symptoms in inflammatory arthropathy. Rheumatoid arthritis often involves the cervical spine, initially causing stiffness and later causing pain.[3] After the hands and feet, the cervical spine is the most common site of disease involvement in rheumatoid arthritis.[5] Ankylosing spondylitis often affects the entire axial skeleton with early limitation of lumbar motion and chest expansion and later involvement of the cervical spine.[3] Fever, night pain and weight loss are suggestive of infectious etiology.

Dyspnea can be related to a deficit in the C3–C5 innervations of the diaphragm. Palpitations and tachycardia secondary to cervical spine pathology can be differentiated from other causes by the fact that these symptoms are associated with unusual positions or hyperextension of the neck. This hyperextension is caused by irritation of C4 innervation of the diaphragm and pericardium or by irritation of the cardiac sympathetic nerve supply. Drop attacks suggest posterior circulation insufficiency.[3] Severe night pain, anorexia, progressive myelopathy is associated with malignancy.

Eye and ear symptoms may arise from irritation of the plexus surrounding the vertebral and internal carotid arteries. Eye

symptoms can manifest with blurring of vision relieved by changing neck position. Altered equilibrium with associated gait disturbances may result from irritation of the surrounding sympathetic plexus or from vertebral insufficiency.

OCCUPATIONAL HISTORY

Jobs requiring hyperextension of neck for overhead work are prone to occipital neuralgia and cervicogenic headache due to upper cervical spine involvement, whereas jobs requiring prolonged neck flexion such as computer work is prone to interspinous ligament sprain and lower cervical spine involvement.

FAMILY HISTORY

Various inflammatory and non-inflammatory arthritis such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome and psoriatic arthritis runs in families and also tumors like schwanoma, neurofibromas, compressing cervical cord seen in familial neurofibromatosis type 1.[1] Family history of diabetes, hypothyroidism will help to identify diabetic neuropathy and widespread pain.

REVIEW OF OTHER SYSTEMS

For diagnosing referred pain from heart, lungs, abdomen, history regarding these systems involvement must be taken thoroughly. Angina can lead to referred neck pain with breathlessness on exertion, and dysrhythmias. In C6–C7 lesion, pain and tenderness may be present in the scapular region or over precordium known as Pseudoangina[3], and may be associated with torticollis or muscle spasm in the neck. Differentiation of heart disease from symptoms associated with C6–C7 dysfunction is made on the basis of muscle weakness, fasciculations and sensory or reflex changes.[6] Respiratory infections can lead to cervical lymphadenopathy causing neck pain. Diaphragmatic irritation due to peritonitis due to infection or abdominal carcinoma will lead to referred pain to shoulder and neck.

PAST TRAUMA AND SURGICAL HISTORY

History of accident with whiplash injury due to hyperextension followed by hyperflexion is significant as these injuries in acute cases should be carefully evaluated for unstable fractures and cord compression. Mostly there is myofascial pain which will recover gradually. The prevalence of cervical facetogenic pain is high in the whiplash population.[7] Past history of trauma or nerve injury with pain more than inciting injury along with sympathetic and autonomic changes, can be suggestive of CRPS. In case of past cervical spine surgery, facet joints and disc above and below fixation are more prone for arthropathy and degeneration due to shifting of load.

EXAMINATION

Clinical examination related to neck pain starts as soon as patient enters the room.

Gait: It is normal when neck pain is due to local pathology not involving cord. In cervical myelopathy, Trendelenburg gait, bilateral spastic, ataxic or spastic-ataxic gait can be present.

Body habits: Cancer patient will be cachexic. Patient with chronic infection will be thin built.

Higher functions: Mood and affect are altered due to chronic pain and help us to know impact of pain on daily routine quality of life. Cognition is impaired in cancer, vascular dissection and hemodynamically unstable patients.

INSPECTION

a. **Skin:** Skin over neck and upper limb is inspected for post-herpetic vesicular scaring which will be dermatomally distributed and do not cross midline in cases of post herpetic neuralgia. Psoriatic skin eruptions can be seen in psoriatic arthropathy. Signs of inflammation like erythema, swelling, redness can be present in local pathologies of neck.

b. Head and neck posture: Patient with neck pain tries to stabilize joint by surrounding muscle contraction to avoid movement aggravating pain.

c. Shoulder symmetry: In cases of shoulder pathologies or neck muscles contraction in myofascial pain, shoulder joints will be drooped or pulled upward.

d. Muscle wasting: Gross muscle wasting can be seen on inspection suggestive of motor nerve fiber involvement like brachial plexopathy. It will be present in both upper and lower limb in case on myelopathy.

PALPATION

It helps us to locate exact pain generators by eliciting local tenderness. Axial cervical spinous tenderness may be present in bilateral facet joint arthropathy, whereas interspinous tenderness in case of interspinous ligament sprain. Paramedial pain may be due to facet joint, myofascial or local infective sources like lymph node. Table 11.3 shows various structures to be palpated anteriorly and posteriorly.

Table 11.3: Palpation findings in a neck pain[1,3]

Anteriorly or anterolaterally	
A. Bony structure	*B. Soft tissue palpation*
1. Between the angle of the jaw and the styloid process—transverse process of C1	1. Thyroid gland swelling or nodule.
2. At the level of the hyoid bone–C3–C4 facet joint.	2. Cervicle lymph nodes enlargement due to infection or metastasis.
3. At the level of the thyroid cartilage–C4–C5 vertebral body and facet joint.	3. Sternocleidomastoid muscle for trigger and tender point.
4. At the level of the cricoid ring—C6 with carotid tubercle.	
5. Head of first rib with 1st costochondral joint should be palpated for pain generator.	
Posteriorly and posterolaterally	
A. Bony structures	*B. Soft tissue palpation*
1. Occiput, inion, superior nuchal line, mastoid processes. Tenderness or pain with examination 3 cm from the midline over superior nuchal line may be seen with occipital neuralgia where greater occipital nerve lies and lesser occipital nerve lies over medial two-thirds and lateral one-third of line joining occiput and mastoid process.	1. Suboccipital muscles and trapezius muscle for myofascial trigger and tender points.
2. Facet joints are located 2–3 cm from the midline. Palpation of the lateral atlantoaxial joint of Cl–C2 is undertaken by rotating the patient's head to the ipsilateral side.[1]	2. Paraspinal muscles for stiffness.
3. C3, C4, C5 are difficult to palpate due to cervical lordosis and identified by anterior structure.	3. Interspinous space for ligament sprain.
4. C7 has a largest spinous process and easily palpated.	4. Posterior group of lymph node for malignant metastais or infection.

RANGE OF MOTION

It may reveal pain or limitations in flexion-extension, lateral bending, and rotation. Neck flexion occurs with 50% of the motion occurring at the occiput-C1 joint and the remaining 50% distributed over C2–C7. If the patient is unable to place the chin on the chest, the interval should be measured. One finger width shows a limitation of 10 degrees; three finger indicates a 30-degree limitation in flexion. Backward neck extension, the distance between the base of the occiput and T1 spinous process should be measured. Lateral flexion should allow the ear to touch the shoulder with motion being shared across all cervical vertebrae. On rotation, the chin should touch the shoulder with 50% of rotation occurring at C1–C2 and the remaining 50% distributed in the sub-axial spine between C3 and C7.[3] There is a natural decrease in range of motion with age, even in healthy individuals.[8] Range of motion tests the ligaments, capsules, and fascia, and this range of motion is reduced in the presence of cervical spinal muscular spasm or pain. Patients with degenerative changes of the cervical spine have pain with decreased range of motion of the cervical spine. The most common findings secondary to changes in the cervical spine articulations are: Restriction of movement with or without pain, pain on movement, and local tenderness. Lateral flexion is the earliest and most impaired movement in degenerative diseases with rotation first impaired in rheumatoid arthritis owing to involvement of the odontoid peg. A uniformly stiff neck may be caused by diffuse idiopathic skeletal hyperostosis, which is present in a quarter of elderly patients, but also may be due to ankylosing spondylitis or recent trauma to the neck.[9] If articular signs are found, the examiner must evaluate the entire vertebral column and peripheral joints for evidence of further arthritis and search for extra-articular manifestations. Causes of decreased range of motion of the cervical spine include joint locking and bony ankylosis from degenerative changes or arthritis, fibrous contractures, muscle spasm, splinting over painful joints, and nerve root or spinal cord compression or irritation.[3]

SPECIAL TESTS AND SIGNS

These tests changes the diameter of the neural foramen, thereby increasing or decreasing the symptoms.

a. **Spurling maneuver** (Fig. 11.1): Passive lateral flexion and compression of head. Positive test is reproduction of radicular symptoms distant from neck.[10] It also increases pressure on the cervical facet joints and may intensify facet mediated pain.[1]

b. **Shoulder abduction (relief) sign** (Fig. 11.2): Active abduction of symptomatic arm, by placing the patient's hand on head. Positive

Fig. 11.1: Spurling's test

Fig. 11.2: Shoulder abduction (relief) sign

test is relief or reduction of ipsilateral cervical radicular symptoms.[1]

c. **Neck distraction test** (Fig 11.3): Examiner grasps patient's head under occiput and chin and applies axial traction force for 30 to 60 seconds. Positive test is relief or reduction of cervical radicular symptoms.[5] Increased pain with this maneuver may be due to inflammatory or degenerative disease, or muscle or ligamentous pathology.[1]

d. **Valsalva test** (Fig. 11.4): This test is performed by having the patients place their thumb in their mouth and blow, as if to push the thumb out of their mouth. This maneuver increases the intraspinal pressure and may reveal the presence of space-occupying lesions of the cervical spine such as large intervertebral disk herniations, tumors, and stenosis due to spondylosis or osteophytes. If the mass involves the area of the spine adjacent to nerve roots, radicular pain may be reproduced.[1]

e. **Jackson's compression test** (Figs 11.5 and 11.6): The patient is instructed to rotate his or her head first to the right and then to the left. The examiner exerts gentle pressure to the top of the patient's head after each movement. This test places increased pressure on the cervical facet joints and causes narrowing of the neural foramen and reproduce neck pain due to facet arthropathy and/or upper extremity radicular pain due to nerve root compression.[1]

Fig. 11.3: Neck distraction test

Fig. 11.5: Jackson's compression test

Fig. 11.4: Valsalva test

Fig. 11.6: Jackson's compression test

f. **Lhermitte's sign:** Production of paraesthesias or dysesthesias in the arms or legs upon flexion of the cervical spine. It may be caused by a large disc herniation or bony compression of the anterior cord in patients with a narrowed central canal. It may also occur in patients with rheumatoid arthritis with associated instability or in patients with multiple sclerosis affecting the cervical spinal cord, tumors, and syringomyelia.[1] This indicates changes in the white matter of the spinal cord and may be secondary to cervical myelopathy or multiple sclerosis.[3]

g. **Adson's maneuver** (Fig. 11.7): This test is used to rule out compression of the subclavian artery by an extra cervical rib or scalene muscle bands, which may result in thoracic outlet syndrome. The patient's arm hangs at their side and the head is extended and rotated toward the affected side. The patient is then instructed to breathe deeply and hold their breath while the radial pulse is monitored. The test is considered positive if the radial pulse disappears[1].

h. **Grip-release test:** It is an inability to open and close a fist rapidly because of weakness and spasticity of the hand.

Sensory Examination

Light touch, pressure sense, pin prick along with temperature and proprioception should be done in both upper limb for comparisons in cases of radiculopathy, CRPS, peripheral neuropathy and in all four limbs in case of myelopathy. Progressive sensory loss is considered as red flag.

Fig. 11.7: Adson's maneuver

Motor Examination

Motor functions are tested as per standard grading 0 to 5, with grade 0 having no power, grade 1 having trace flickering movements, grade 2 having motion with gravity eliminated, grade 3 having antigravity function, grade 4 having function against slight resistance, and grade 5 having normal strength against resistance. Progressive decreasing motor grading or grade 3 or less is considered as red flag. Lower motor neuron disease is indicated by weakness, hypotonia, and fasciculations. Upper motor neuron disease is indicated by spasticity.[3]

Reflexes

Deep tendon stretch reflexes should be performed and graded on a scale of 0 to 3 with 0 being no response, 1 being hyporeflexive, 2 being normal, and 3 being hyperreflexive. To facilitate reflex testing, it may be helpful to use muscle loading or Jendrassik maneuver (performed by having the patient flex both sets of fingers into a hook like form, interlocking the hands, and pulling apart). This maneuver creates a diversion to help relax the patient and assess lower extremity reflexes. If difficulty with reflex testing persists, the clinician should ensure that no peripheral neuropathy is present.[3]

a. **Biceps reflex** (Fig. 11.8): C5 is tested by striking the biceps tendon with elbow flexed.

b. **Supinator reflex** (Fig.11.9): C6 mediated and tested with elbow semi-flexed with forearm midpronated by striking over brachioradialis tendon over radial tubercle.

c. **Triceps reflex** (Fig. 11.10): C7 mediated and tested with elbow flexed and triceps tendon is striked above olecranon process.

Fig. 11.8: Biceps reflex

Fig. 11.9: Supinator reflex

Fig. 11.10: Triceps reflex

d. Babinski test: It is performed by stroking the lateral plantar aspect of the foot with a pathologic response indicated by an up-going great toe indicating an upper motor neuron lesion.[10]

Lower limb reflexes, knee and ankle reflex should be checked in case of myelopathy in which they will be exaggerated due to upper motor neuron lesion, where as upper limb reflexes will be diminished due to lower motor neuron lesion.

OTHER SYSTEMIC EXAMINATION

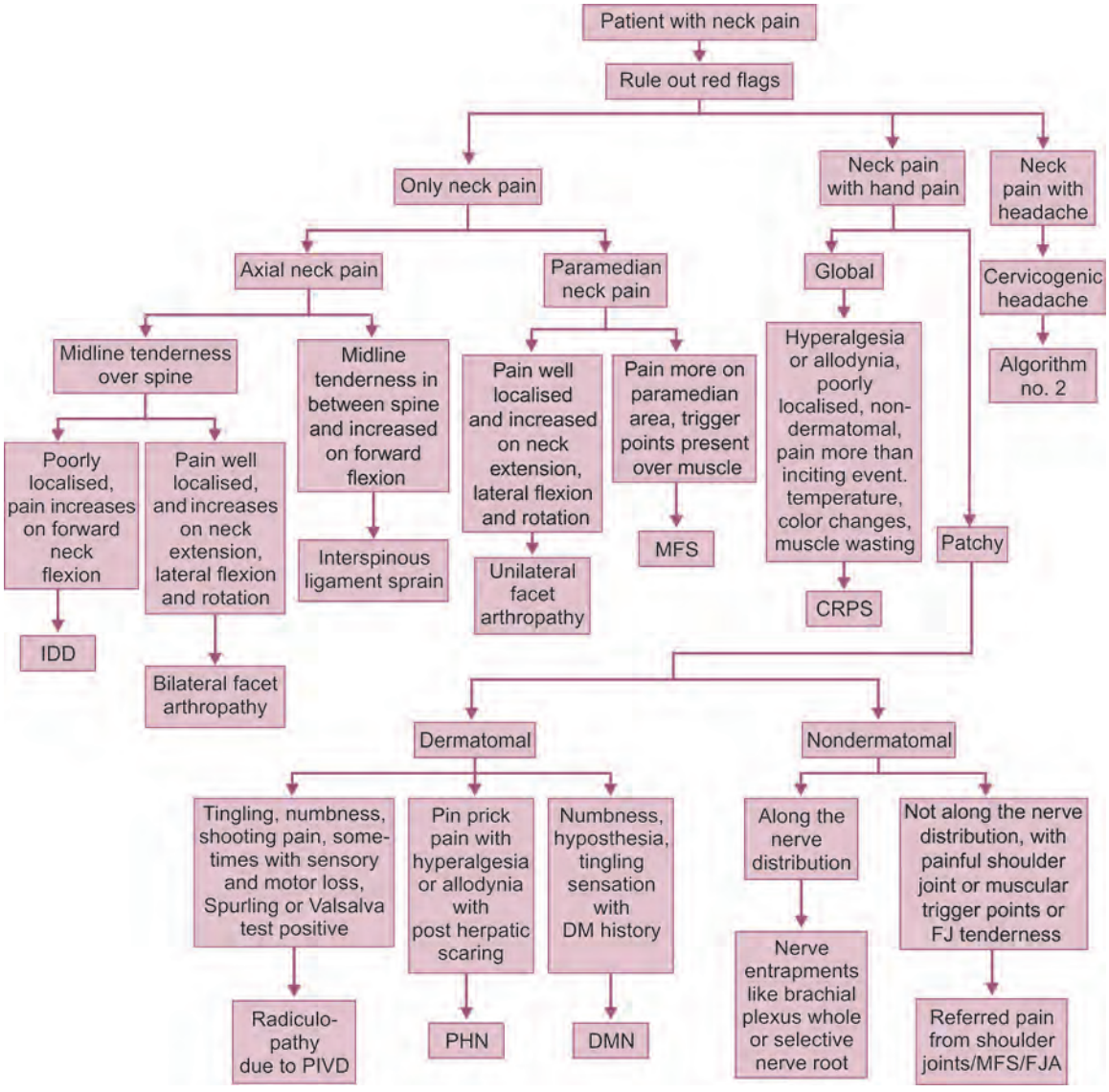
a. Cardiovascular: To rule out referred pain of angina in neck, cardiovascular examination must be carried out thoroughly

b. Respiratory: Pancoast tumor of lung apex causes lower brachial plexus invasion and plexopathy, diaphragmatic involvement can cause referred neck pain. Respiratory rate, pattern and lung field auscultation helps to rule out lung pathologies.

c. Abdominal: Palpation of abdominal organs for enlargement and infection.

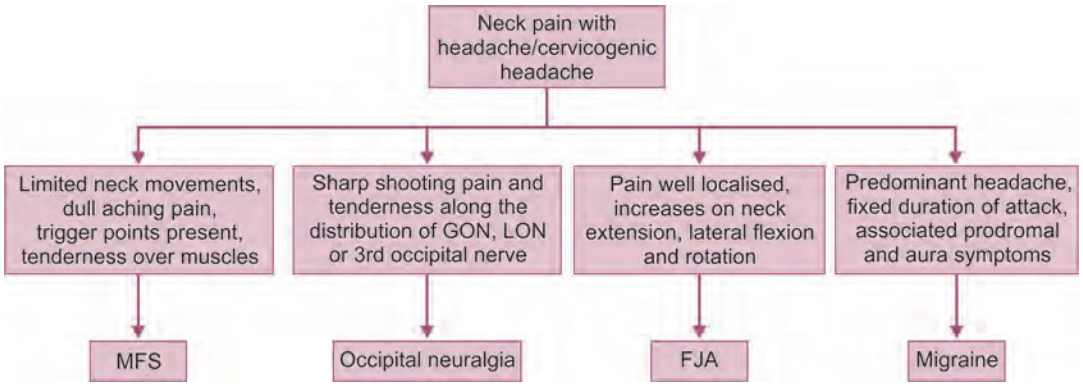
DIAGNOSTIC ALGORITHMS OF NECK PAIN

Algorithm 1


Patient with neck pain
Rule out red flags
Only neck pain
Neck pain with hand pain
Neck pain with headache
Axial neck pain
Paramedian neck pain
Global
Cervicogenic headache
Midline tenderness over spine
Midline tenderness in between spine and increased on forward flexion
Pain well localised and increased on neck extension, lateral flexion and rotation
Pain more on paramedian area, trigger points present over muscle
Hyperalgesia or allodynia, poorly localised, non-dermatomal, pain more than inciting event. temperature, color changes, muscle wasting
Algorithm no. 2
Poorly localised, pain increases on forward neck flexion
Pain well localised, and increases on neck extension, lateral flexion and rotation
Interspinous ligament sprain
Unilateral facet arthropathy
MFS
CRPS
Patchy
IDD
Bilateral facet arthropathy
Dermatomal
Nondermatomal
Tingling, numbness, shooting pain, sometimes with sensory and motor loss, Spurling or Valsalva test positive
Pin prick pain with hyperalgesia or allodynia with post herpatic scaring
Numbness, hyposthesia, tingling sensation with DM history
Along the nerve distribution
Not along the nerve distribution, with painful shoulder joint or muscular trigger points or FJ tenderness
Nerve entrapments like brachial plexus whole or selective nerve root
Radiculopathy due to PIVD
PHN
DMN
Referred pain from shoulder joints/MFS/FJA

MFS—Myofascial pain syndrome, FJA—facet joint arthropathy, IDD—internal disc disruption, PIVD—prolapse intervertebral disc, PHN—postherpetic neuralgia, DMP—diabetic mononeuropathy, CRPS—complex regional pain syndrome.

Algorithm 2


Neck pain with headache/cervicogenic headache
Limited neck movements, dull aching pain, trigger points present, tenderness over muscles
Sharp shooting pain and tenderness along the distribution of GON, LON or 3rd occipital nerve
Pain well localised, increases on neck extension, lateral flexion and rotation
Predominant headache, fixed duration of attack, associated prodromal and aura symptoms
MFS
Occipital neuralgia
FJA
Migraine

MFS—myofascial pain syndrome, FJA—facet joint arthropathy, GON—greater occipital nerve, LON—lesser occipital nerve.

REFERENCES

1. Fishman SM, Ballantyne JC, Rathmell JP. Bonica's management of pain; 4th ed; Philadelphia; Lippincott Williams & Wilkins, Wolters Kluwer; 2010; p.1020–28.
2. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al (eds). Harrison's principles of internal medicine; 18th ed; New York; McGraw Hill; 2012.p.140.
3. Gary S. Firestein GS, Ralph C. Budd, Gabriel SE, O'Dell JR, McInnes LD. Kelley's Textbook of Rheumatology; 9th Edition; Philadelphia; Elsevier; 2013.p.628–37.
4. Kelley WN, Harris ED Jr, Ruddy S, et al (eds). Textbook of Rheumatology; 5th ed. Philadelphia, WB Saunders. 1997; p 394.
5. Crockard HA. Surgical management of cervical rheumatoid problems. Spine. 1995; 20: 2584–90.
6. Frobert O, Fossgreen J, et al. Musculoskeletal pathology in patients with angina pectoris and normal coronary angiograms. J Intern Med 1999; 245: 237–46.
7. Hans van Suijlekom, Nagy Mekhail, Nileshkumar Patel, Jan Van Zundert, Maarten van Kleef, Jacob Patijn: Pain practice. 2010; 10(2):131–6.
8. Sforza C, Grassi G, et al. Three-dimensional analysis of active head and cervical spine range of motion: Effect of age in healthy male subjects; Clin Biomech (Bristol, Avon) 2002; 17: 611–4.
9. Weinfeld RM, Olson PN, et al. The prevalence of diffuse idiopathic skeletal hyperostosis (DISH) in two large American Midwest metropolitan hospital populations. Skeletal Radiol; 1997; 26: 222–5.
10. Waldman SD. Pain Management. 2nd ed. Philadelphia; Elsevier, Saunders; 2011; p.526.

CHAPTER

12

Management of Neck Pain

Rammurthy and Ravi Shankar Sharma

1. TREATMENT OF ACUTE NECK PAIN

Just like acute low back pain, acute neck pain also has a favorable prognosis, where up to 40% of patients recover fully from neck pain and about 30% of patients will continue to have mild symptoms.[1] Hence the treatment of acute neck pain should not be aggressive in the absence of red flags. In fact a multivariate analysis showed that the highest rate of recovery from the neck pain was seen in those cases where the treating general practitioners adapted a conservative "wait and see" approach than in those cases where the cases were referred to a specialist for additional management.[2]

Pharmacological Management

Although the evidence is poor, analgesics have been used for the symptomatic treatment of neck pain.

Paracetamol, NSAIDs like ibuprofen, naproxen are prescribed to reduce pain and inflammation. Muscle relaxants are used to reduce spasm and spasticity. Opioids like tramadol, codeine are the frequently used drugs in debilitating conditions. Other drugs used are antispastic agents, antidepressants and local transdermal patches.

Non-pharmacological Management[1]

Patients should be advised to stay active and to resume to the normal activities. Staying active helps in speedy recovery compared to the use of cervical collar and rest.

Conventional treatment like physical therapy which includes strengthening and stretching exercises promote an increased range of motion and elasticity in neck muscles.

Gentle neck exercises and active release techniques which are performed at home are quite effective and should be encouraged.

2. MANAGEMENT OF RED FLAGS

Presence of red flag indicates serious underlying pathology and hence there is no role for conservative management. Hence one should not miss to identify the red flags. In case of red flags, imaging of the spine is must and urgent neurosurgical referral is warranted for surgical management like decompression of the space-occupying lesion such as abscess, hematoma, tumor, huge disc prolapse or fixation of vertebral fractures in case of neurodeficits, dislocations and trauma.

3. TREATMENT OF CHRONIC NECK PAIN

When the neck pain persists for more than 3 months with or without treatment, it is called as chronic neck pain. Chronic neck pain responds poorly to conservative treatment and hence invasive treatment like percutaneous interventions are recommended.

1. Medial Branch Block for Facet Joint Pain

Facet joint arthropathy in the cervical region is a common cause of neck pain than in the lumbar region. The pain is usually unilateral,

paramedian, aggravated on neck extension and lateral rotation.[3] Paramedian tenderness over the facet joints is present. As in lumbar region, X-ray or MRI is not diagnostic. Fluoroscopy aided medial branch block with > 50% (80% according to some studies) pain relief is diagnostic. This can be followed by radiofrequency ablation of the medial branches for long-term pain relief.

2. Cervical Epidural Steroid for Cervical Radicular Pain[4]

Cervical radiculopathy is usually caused by prolapsed cervical intervertebral disc. The pain is usually dermatomal depending on the nerve root affected with electric shock like sensation. It is usually associated with tingling and numbness. Cervical interlaminar epidural steroid injection under fluoroscopy is the commonly done procedure for the cervical radicular pain. It provides good pain relief to the patients by reducing inflammation (RE move and pain).

3. Interventions for Myofascial Pain

Myofascial pain of the trapezius muscle is again a common cause of neck pain. The pain is aching type, aggravated by passively stretching the muscle (contralateral neck flexion). Trigger points, taut bands can be palpated within the muscle. Trigger point injections using local anesthetic and steroid produces dramatic relief. Dry needling or intramuscular stimulation are the treatment of choice in chronic cases of muscle spasm and stiffness of neck muscles.

4. ADVANCED PROCEDURES

Pulsed radio frequency on adjacent cervical dorsal root ganglion for cervical radicular pain patients.[5]

Vertebroplasty for compression fracture of vertebra.

Spinal cord stimulation and intrathecal systems are used to treat neck pain in resistant and terminally ill patients.

Surgical interventions—in presence of red flags.

Neck pain is a potentially disabling condition which if not managed early can land up in chronic stage. A number of novel approaches as described can manage the pain effectively.

REFERENCES

1. Evidence based management of acute musculoskeletal pain. A guide for clinicians. Australian Academic Press. Bowen Hills. 2004.
2. Vos CJ, Verhagen AP, Passchier J, Koes BW. Clinical Course and Prognostic Factors in Acute Neck Pain: An Inception Cohort Study in General Practice. Pain Medicine. 2008; 9 (5): 572–80.
3. Van Eerd M, Patijn J, Lataster A, Rosenquist RW, van Kleef M, Mekhail N, et al. Cervical Facet Pain. Pain Practice. 2010; 10 (2):113–23.
4. Van Zundert J, Huntoon M, Patijn J, Arno Lataster A, Nagy Mekhail N, van Kleef M. Cervical radicular pain. Pain Practice. 2010; 10(1): 1–17.
5. Yoon YM, Han SR, Lee SJ, Choi CY, Sohn MJ, Lee CH. The efficacy of pulsed radiofrequency treatment of cervical radicular pain patients. Korean J Spine. 2014;11(3):109-12.

CHAPTER

13

Myths in Neck Pain

Rammurthy

1. **MYTH: MRI of the cervical spine should be advised in all cases of neck pain.**

   FACT: MRI of the cervical spine is indicated only in the presence of red flags.

   This is the most common myth among the treating physicians and the patients that MRI of the cervical spine can detect the cause of the neck pain and hence should be done in each case of neck pain. But the fact is that in most of the cases, abnormal MRI findings are just co-incidental and does not have any relation with the neck pain. Nakasimha et al studied cervical MRI scans of 1211 asymptomatic subjects. They found that >80% of the subjects showed disc bulge in their scans.[1] Similarly Boden et al also studied MRI scans of the cervical spine in 63 asymptomatic volunteers and found that 19 % of the subjects showed abnormal findings.[2] Hence MRI scans are not 100 % diagnostic and hence can be misleading. They unnecessarily increase the cost of the treatment and may even lead to unwanted surgeries.

2. **MYTH: Normal MRI scan of the cervical spine means that the pain is not real.**

   FACT: A normal MRI scan in a symptomatic patient does not mean that there is no spine pathology.[3]

   This is again a big myth that if there are no signs of any abnormality in the MRI of a symptomatic neck pain patient, many treating physicians and surgeons conclude that the pain is not real and everything is just in patient's mind. This can lead to unnecessary psychiatric referral. In fact, MRI cannot reliably identify the source of neck pain particularly the discogenic pain, cervical facet pain and myofascial pain. In these cases the diagnostic interventions are more helpful in confirming the diagnosis rather than imaging modality.

3. **MYTH: Complete rest helps in recovering from neck pain.**

   FACT: Staying active is more helpful than complete rest.

   Prolonged bed rest is not indicated in low back pain. Similarly complete rest is also not indicated in cases of neck pain. Active neck movements within the limits of pain help in faster recovery than prolonged rest.

4. **MYTH: Use of cervical collar helps in reducing the neck pain.**

   FACT: Use of cervical collar is not helpful and may be even harmful.

   Cervical collars (soft collars) are usually prescribed by many physicians and orthopedicians for the treatment of neck pain.[4] Use of these collars for prolonged duration is actually harmful. Initial transient pain relief can be obtained due to immobilization but on a long term use, disuse atrophy of the neck muscles which are the important support of the cervical spine has been reported. Similarly in whiplash associated

disorders,[5] the long-term use of these cervical collars is not recommended and hence should be discouraged. Hard and rigid cervical collars are useful in stabilizing the cervical spine in cases of cervical spine fracture or subluxation/dislocations to prevent further damage.

5. **MYTH: Cervical traction is helpful for cervical radiculopathy.**

FACT: There is insufficient evidence to support the need for cervical traction in cases of cervical radiculopathy. Cervical traction increases the severity of pain tingling and numbness when advised by treating physicians.[6]

According to a Cochrane review, the evidence for the cervical traction in the management of cervical radiculopathy is poor and hence should not be practiced.

REFERENCES

1. Nakashima H, Yukawa Y, Suda K, Yamagata M, Ueta T, Kato F. Abnormal findings on magnetic resonance images of the cervical spines in 1211 asymptomatic subjects. Spine (Phila Pa 1976). 2015 Mar 15; 40(6):392–8.
2. Boden SD, Mc Cowin PR, Davis DO, Dina TS, Mark AS, Wiesel S. Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am. 1990 Sep; 72(8):1178–84.
3. Schellhas KP, Smith MD, Gundry CR, Pollei SR. Cervical discogenic pain. Prospective correlation of magnetic resonance imaging and discography in asymptomatic subjects and pain sufferers. Spine (Phila Pa 1976). 1996 Feb 1; 21(3):300–11.
4. Muzin S, Isaac Z, Walker J, Abd OE, Baima J. When should a cervical collar be used to treat neck pain? Curr Rev Musculoskelet Med (2008) 1:114–9.
5. Gennis P, Miller L, Gallagher EJ, Giglio J, Carter W, Nathanson N. The effect of soft cervical collars on persistent neck pain in patients with whiplash injury. Acad Emerg Med. 1996 Jun; 3(6):568–73.
6. Van Zundert J, Huntoon M, Patijn J, Arno Lataster A, Nagy Mekhail N, van Kleef M. Cervical radicular pain. Pain Practice. 2010; 10(1): 1–17.

IV

SECTION

IV

Headache Management

Ashok Jadon and Ravi Shankar Sharma (Section Editors)

14. Classification and Evaluation of Headache
15. Tension-type Headache
16. Migraine
17. Cervicogenic Headache
18. Cluster Headache
19. Myths in Headache

CHAPTER

14

Classification and Evaluation of Headache

Kanchan Sharma, Gautam Das, Ravi Shankar Sharma and Sunny Malik

INTRODUCTION

Headache also known as cephalgia[1] is one of the common disorders that need medical attention by a neurologist as well as a pain physician.

Headache hampers living of about 64–77% of people at some point of their lives.[2] During each year, on average, 46–53% of people have headaches.[3] Migraine and tension-type headache (TTH) are common primary headache disorders in clinical practice while vascular disorder and infective pathology is common among secondary headache disorders.

Headache can arise from certain extracranial (scalp, muscles, cervical and temporomandibular joints, paranasal sinuses, teeth, ocular contents) as well as intracranial structures (blood vessels, meninges, cranial nerves).

This discussion focuses on classification, evaluation and investigations of the common headache disorders encountered for pain relief in a pain clinic.

CLASSIFICATION

As per International Headache Society Classification, headache is broadly classified into: primary headache where underlying pathology is not known, and secondary headache when headache is attributed to some underlying pathology. However, if primary headache like migraine occurs for the first time in association with another disorder known to cause headache, the new headache will be considered as a secondary headache attributed to the causative disorder.

Nearly about 90 per cent of these benign headache falls under a few category, including migraine, tension type, and cluster headache. Still a few headaches being described for the first time and enough information is not available about them are classified as headache not classifiable or headache not elsewhere classified.

CLASSIFICATION OF HEADACHE

A. The Primary Headache

1. Migraine
2. Tension-type headache
3. Trigeminal autonomic cephalgias
4. Other primary headache disorders:
    i. Primary cough headache
    ii. Primary exercise headache
    iii. Primary headache associated with sexual activity
    iv. Primary thunderclap headache
    v. Cold-stimulus headache
    vi. External-pressure headache
    vii. Primary stabbing headache
    viii. Nummular headache
    ix. Hypnic headache
    x. New daily persistent headache (NDPH)

B. The Secondary Headache

1. Headache attributed to trauma or injury to the head and/or neck
2. Headache attributed to cranial and/or cervical vascular disorder
3. Headache attributed to non-vascular intracranial disorder
4. Headache attributed to a substance or its withdrawal
5. Headache attributed to infection
6. Headache attributed to disorder of homoeostasis
7. Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure
8. Headache attributed to psychiatric disorder
9. Painful lesions of the cranial nerves and other facial pain

C. Other Headache Disorders

1. Headache not elsewhere classified
2. Headache unspecified

HEADACHE: EVALUATION

EVALUATION OF PAIN: HISTORY

Out of all headache majority are benign, however, approximately 1–5% have some serious underlying pathology and must be evaluated with utmost importance for early recognition and management of severe underlying pathology. Careful history is necessary in the evaluation of headache disorders as most of the primary headache disorders reveal a normal physical and neurological examination. Detailed history helps in classifying as well as diagnosing headache disorders. The usual features of a few common headache are given in Table 14.1. Pain diaries are also a useful tool

Table 14.1: The usual features of common headache disorders

Headache history	*Migraine*	*Tension headache*	*Cluster headache*	*Secondary headache*
Age	Childhood/early adult life	Early adult life and adolescents (young age)	Childhood/early adult life	New onset at any age/old age
Location	U/L usually but can be B/L. Often fronto-temporal	B/L band like/in whole head, radiates from occiput to frontal region	U/L usually affecting orbit, bridge of nose or nearby areas	Pain tracking down spinal column towards lower back, e.g. SAH
Intensity	Moderate to severe: Pounding or throbbing	Mild to moderate that comes and goes	Very severe and unbearable	Sudden onset severe headache
Progression	Lasts from hours to three/four days	Chronic daily headache	Occur in clusters. Remission period of months to years	Thunderclap headache in vascular etiologies like SAH, pituitary apoplexy and cerebral vasocon-striction syndrome
Character	Pulsatile or throbbing type	Band like, aching or holocephalic pressure type	Drilling, lancinating or boring type. Patient is restless	Burning and pulsatile type in vascular insults

Contd.

Table 14.1: The usual features of common headache disorders (Contd.)

Headache history	*Migraine*	*Tension headache*	*Cluster headache*	*Secondary headache*
Duration	Recurrent headache lasting 4–72 hours	Occur almost daily and may last from 30 minutes up to 7 days	Occur in clusters with periods of weeks to months between new cluster period	Occurs in close relation to other aetiology. Headache is greatly reduced within 3 months after treatment of underlying disorder
Frequency	1–4 attacks per month	At least 10 episodes occurring on <1 day per month on average (<12 days per year)	1–8 attacks per day	Causal relationship
Provocating and relieving factors	Menses, ovulation, hunger, lights, perfumes, environmental factors, etc. Relieved by rest in dark room	Stress increases pain. Rest and meditation reduces tension headache	Certain vasodilators like nitroglycerine, alcohol and histamine triggers pain.	ICP hypertension increased by changing posture. Third ventricle cyst and Arnold-Chiari headache increased by cough/Valsalva
Premonitory symptoms and aura	Occur in migraine with aura: Visual, aural, flashes, floaters, paraesthesia, hyperesthesia, etc. Depression, certain foods, frequent yawning, fatigue and altered sleep predict its arrival	Photophobia or phonophobia may occur	Ipsilateral lacrimation, eye/nasal congestion, lid oedema, miosis, ptosis. Patient is agitated and moves to and fro	Completely new headache. Neurological symptoms present.
Daily activities	Associated nausea/vomiting and pain affects day to day activities	Anorexia may occur	Sense of restlessness and agitation during the attacks	May be hampered in patients with neurological signs and symptoms

U/L, Unilateral; B/L, Bilateral; SAH, Subarachnoid hemorrhage

and can help to identify headache patterns and triggers.

Family history is important in familial hemiplegic migraine, cerebral aneurysms and brain tumors as they show some genetic influence and run in families. History related to drug intake is very important as certain medications such as hormone replacement therapy, oral contraceptive pills, nitroglycerine, antihistaminic, etc. could be a reason for causing headache. Excessive use of analgesics may cause medicine overuse headache in chronic primary headaches.

History of head trauma, repeated infections, substance abuse, depression and sleep disorders should be asked while evaluating secondary headaches.

Alcohol, caffeine, cannabis and cocaine are some examples implicated with substance abuse associated headache.

Presence of Yellow flags (Table 14.2) in history also warrant attention.

Table 14.2: Yellow flags of headache

Yellow flags	*Concerns and significance*
Headache causing waking up of the patient	Common in migraine, paroxysmal hemicrania, and cluster headache, poorly controlled essential hypertension can also lead to nocturnal or morning headache. American Academy of Neurology (AAN) practice parameter recommends consideration of brain imaging for these patients.
New onset side-locked headaches (always occur on the same side) Postural headaches	Suggest an anatomical mechanism which may be a symptom of intracranial pathology. If primary unilateral headache is ruled-out, patients should be further investigated. It is an important yellow flag indicates intracranial pathology and patients has to investigated further. Appropriate evaluation includes MRI of the brain with and without contrast.

EXAMINATION: GENERAL

General physical, neurologic and systemic examination is done to rule out certain red flags and atypical headaches. Further investigations and neuroimaging are warranted in case any abnormality is encountered during examination.

In general examination, look for general body habitus. Obesity is usually associated with migraine. A high blood pressure points towards hypertensive encephalopathy in extreme situations. Temperature should be measured as fever points towards some infective pathology. Fever associated with nuchal rigidity and redness around temporal region raises suspicion of meningitis, encephalitis or giant cell arteritis. Weight loss may be associated with tubercular and malignant pathology. Skin changes may be associated with a variety of aetiologies for headache. Café-au-lait spots suggest neurofibromatosis associated with intracranial meningiomas and schwannomas. Dermatomal distribution and scar of Herpes zoster neuralgia should also be noted.

SYSTEMIC EXAMINATION

Higher functions are examined in terms of memory, speech, concentration and orientation (time, place and person). Higher functions are frequently normal with primary headaches. A mini mental scale is a good quality tool for assessing higher functions. Memory can be impaired in head trauma, stroke and temporal lobe tumor.

Slurring of speech can be associated with migraine aura but is completely reversible once the attack resolves. Other speech disturbances occur in ischemic infarcts and brain space occupying lesions.

Inspect the face, head and neck to rule out any obvious local inflammation or infective pathology. Remember redness of eyes, lacrimation, lid edema and facial sweating occur in cluster headache only during the attacks.

Palpate for trigger points (tender nodule or taut band) in cervical region as cervical facet arthropathy and myofascial pain syndromes are common in the neck that can produce headache. Tapping over trigeminal nerve distribution results in pain in cases of neuralgias. The only positive finding on examination in primary tension headache can be tenderness over the scalp. Examination of temporomandibular joint is important especially in gutka chewers, as evident by decreased mouth opening, reduced mastication and tender points in the region of TMJ. This clearly indicates TMJ arthropathy.

Auscultation of Bruits over carotid or vertebral arteries points toward some vascular

pathologies such as arterial dissection or AV malformations. Congenital heart diseases predispose the patients to brain abscesses.

Central nervous system examination is vital in every headache patient and helps to rule out red flags (Table 14.3). If patient has neck stiffness (**Nuchal rigidity)** along with severe headache, it indicates presence of meningeal inflammation. Use of algorithm (Fig. 14.1) to evaluate any patient with headache helps in early decision making and proper management.

Table 14.3: Red flags in headache

Red Flags	*Possible causes*	*Diagnostic tests*
New headache after age 50	Temporal arteritis Brain mass Giant cell arteritis	Erythrocyte sedimentation rate (diagnostic test for temporal arteritis), neuroimaging
Very sudden onset headache (thunderclap headache)	Brain bleed, Vascular malformation, pituitary apoplexy, mass (especially in posterior fossa)	Neuroimaging Lumbar puncture if computed tomography is negative
Headaches increasing in frequency and severity	Mass Subdural hematoma Medication overuse	Neuroimaging Drug screen
New onset headache in a person with possible HIV or cancer	Meningitis (chronic or carcinomatous) Brain abscess	Neuroimaging Lumbar puncture, if neuroimaging is negative
Headache with signs of total body illness (fever, stiff neck, rash)	Meningitis Encephalitis Collagen vascular disease	Neuroimaging Lumbar puncture Serology for infections
Papilledema	Brain mass Benign intracranial hypertension Meningitis Encephalitis	Neuroimaging, lumbar puncture
Severe headache following head trauma	Brain bleeds (intracranial hemorrhage, subdural hematoma, epidural hematoma)	Post-traumatic headache Neuroimaging of brain skull, and possibly cervical spine
Inability to move a limb (neurologic sign and symptoms)	Arteriovenous malformation Collagen vascular disease Intracranial mass lesion	Neuroimaging Blood tests for collagen vascular diseases
Change in personality, consciousness, or mental status	Central nervous system infection, intracranial bleed, mass	Blood tests, lumbar puncture, neuroimaging
Headache triggered by cough, exertion or while engaged in sexual intercourse	Mass lesion Subarachnoid hemorrhage	Neuroimaging, lumbar puncture
Metabolic disorders	Thyroid disorders Vitamin B_{12} deficiency Cushing syndrome	Blood tests
Toxic ingestion	Carbon monoxide Drug exposure (triptans, opioids, barbiturates, NSAIDs, caffeine)	Blood levels

INVESTIGATIONS[5]

Investigations are generally normal in the vast majority of primary headache. Although a thorough history and examination usually lead us to diagnosis, certain tests are done to rule out secondary headache, atypical headache and red flags.

Blood investigations are done to rule out infections, diabetes mellitus and thyroid disorders that can trigger headache. Traumatic fractures of the skull and cervical spine pathology are ruled out on X-ray skull and neck. A minimal imaging technique in the form of an X-ray should be available before going for any diagnostic block in the region of the head and neck from the medicolegal point of view. Sinus X-ray might be needed if sinus problems are considered. X-ray Chest is needed in suspected tubercular pathology and bronchogenic carcinomas.

Neuroimaging is generally considered to rule out some intracranial pathology leading to positive finding such as weakness encountered during examination.

There is a lack of any definitive data or guidelines regarding neuroimaging for diagnosis of headache. It can be considered in:

- Recent significant change in the pattern, frequency, or severity of headache
- Progressive worsening of headache despite appropriate therapy
- Focal neurologic signs or symptoms
- Onset of headache with exertion, cough, or sexual activity
- Orbital bruit

There is lack of evidence to make some clear cut guidelines for the use of neuroimaging for headache evaluation. CT scan is cheaper than MRI, easily available in the emergency department and can be used to rule out any intracranial bleed. MRI have the definite advantage in ruling out soft tissue lesions and are commonly implicated in vascular and space occupying lesions of posterior fossa.

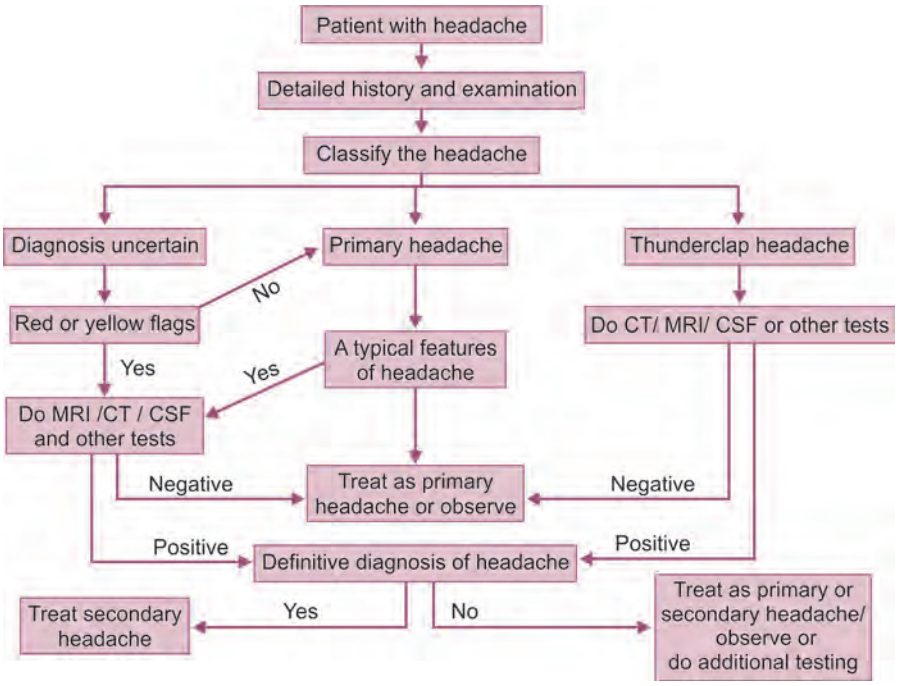


Fig. 14.1: Algorithm for evaluation of patient with headache

Magnetic resonance angiography and venography are sophisticated non-invasive measures to delineate the craniocerebral circulation. They are particularly useful in suspected aneurysm and AV malformation. They are helpful in cerebral venous thrombosis as well as in detecting trigeminal nerve root compression due to any vascular loop.

EEG has low weightage during headache evaluation but can be helpful in patients with suspicion of epilepsy.

Thunderclap headache that is severe and progressive with a normal CT scan needs further evaluation with a lumbar puncture. It is done in suspected subarachnoid hemorrhage, high/low CSF pressure headache and meningoencephalitis along with seizures, fever, confusion and signs of meningism. Xanthochromia after CSF centrifugation points towards subarachnoid bleed.

Certain diagnostic blocks tried in headache disorders are as follows:

1. Occipital neuralgia: Occipital nerve block
2. Trigeminal neuralgia: Gasserian ganglion block
3. Cluster headache: Sphenopalatine block
4. Cervicogenic headache: C2-3 medial branch block
5. Myofascial pain syndrome (cervical and scapular): Trigger point injection
6. Internal disc disruption or pain of radiculopathy: Cervical epidural

Conclusion

To conclude, a systematic approach to a patient with headache through history and examination added with their individual diagnostic criteria is must. This helps us in reaching to a diagnosis and finding out red flags if any that needs urgent referrals and further investigations.

REFERENCES

1. 1.The International Classification of Headache Disorders. Cephalalgia. 2018; 38 (3rd edition):1–211.
2. Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population—a prevalence study. J Clin Epidemiol. 1991; 44:1147–57.
3. Manzoni GC, Stovner LJ . Epidemiology of headache. Handbook of Clinical Neurology 2010;97: 3–22.doi:10.1016/s0072–9752(10) 97001-2. ISBN 978-0-444-52139-2. PMID 20816407.
4. The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2013; 33(9) 629–808.
5. De Luca GC, Bartleson JD. When and How to Investigate the Patient with Headache. Seminars in neurology 2010;30 (2):131–44.

CHAPTER

15

Tension-type Headache

Ravi Shankar sharma and Mousumi Datta

Tension-type headache (TTH) is most prevalent form of primary headache (30–78%) affecting both sexes. It is commonly used to describe a chronic headache syndrome characterized by bilateral tight, band-like discomfort. Though the name suggests tension, there is no clear evidence for tension as an aetiology however; peripheral, central and genetic factors are supposed to be responsible factors. It involves all age groups and has varied presentations, therefore, posing diagnostic difficulties.

Characteristics

- Female preponderance
- Episodic (<15d/month) or chronic (≥15d/month)
- Bilateral or unilateral (frontal, temporal or occipital regions)
- Constant band-like, non-pulsatile ache or tightness
- Mild to moderate but may be severe in chronic forms
- Increased headache with muscle activity (chewing)
- May be associated with or without pericranial muscle tenderness (frontal, temporal, masseter, pterygoid, sternocleidomastoid, splenius and trapezius muscles)
- No exertional exacerbation
- May be associated with either photophobia or phonophobia but not both
- Not associated with nausea/aura/premonitory symptoms
- Co-existing conditions: Cervical spondylosis, sleep disturbances, anxiety, depression, TMJ syndrome

Diagnostic criteria

Infrequent episodic tension-type headache:

A. At least 10 episodes of headache occurring on <1 day/month on average (<12 days/year) and fulfilling criteria B–D
B. Lasting from 30 minutes to seven days
C. At least two of the following four characteristics:
   1. Bilateral location
   2. Pressing or tightening (non-pulsating) quality
   3. Mild or moderate intensity
   4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
   1. No nausea or vomiting
   2. No more than one of photophobia or phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Frequent episodic tension-type headache

Diagnostic criteria:

A. At least 10 episodes of headache occurring on 1–14 days/month on average for >3 months (12 and <180 days/year) and fulfilling criteria B–D
B. Lasting from 30 minutes to seven days
C. At least two of the following four characteristics:
   1. Bilateral location
   2. Pressing or tightening (non-pulsating) quality
   3. Mild or moderate intensity
   4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
   1. No nausea or vomiting
   2. No more than one of photophobia or phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Chronic tension-type headache

Diagnostic criteria:

A. Headache occurring on 15 days/month on average for >3 months (180 days/year), fulfilling criteria B–D
B. Lasting hours to days, or unremitting
C. At least two of the following four characteristics:
   1. Bilateral location
   2. Pressing or tightening (non-pulsating) quality
   3. Mild or moderate intensity
   4. Not aggravated by routine physical activity such as walking or climbing stairs
D. Both of the following:
   1. No more than one of photophobia, phonophobia or mild nausea
   2. Neither moderate or severe nausea or vomiting
E. Not better accounted for by another ICHD-3 diagnosis.

Diagnosis

A detailed history and thorough examination of the head and neck usually points to the diagnosis. Pericranial muscle tenderness and neck symptoms along with sleep disturbances gives a clue to the diagnosis. It is usually associated with psychological disorders like anxiety and depression which may also aid in the diagnosis. Neuroimaging of the head and neck are negative for any findings and should be considered in excluding differential diagnoses.

Differential Diagnosis

- Migraine (migraine without aura, chronic migraine) (Table 15.1)
- Medication overuse headache
- TMJ syndrome
- Nasal sinusitis
- Disorders of the eyes
- Musculoskeletal disorders (fibromyalgia, arthritis)

Frequent episodic tension-type headache often coexists with migraine without aura. Coexisting tension-type headache in patients with migraine should be identified through use of a diagnostic headache diary. The treatment of migraine differs considerably from that of tension-type headache, and it is important to educate patients to distinguish between these headache types if they are to select the right treatment for each while avoiding medication overuse and the adverse consequences of medication overuse headache.

Table 15.1: Comparison of tension-type and migraine headache

	Tension-type headache	*Migraine headache*
Onset-to-peak interval	Hours to days	Minutes to 1 hr
Frequency	Often daily or continuous	Rarely > 1/wk
Localization	Nuchal or circ-umferential	Temporal
Character	Aching, pressue, band-like	Pounding
Laterality	Usually bilateral	Always unilateral
Aura	Never present	May be present
Nausea and vomiting	Rare	Common
Duration	Often days	Usually < 24 hr

Treatment of TTH

Treatment of Acute Attack

Aspirin and Paracetamol are recommended for the acute treatment of tension type headache. Other NSAIDs and caffeine can also be used but opioids are not recommended.

Prophylaxis

Antidepressants

Tricyclic antidepressants, particularly amitriptyline, 25–150 mg per day, is recommended as the agent of choice where prophylactic treatment is being considered in a patient with chronic tension-type headache.

Anti-hypertensives

High blood pressure does not usually cause headache, although blood pressure lowering

treatments can reduce the prevalence of headache.

Anti-epileptics

Gabapentin has been shown to relieve symptoms in patients with chronic daily headache.

Other Options

- Relaxation therapies
- Exercises
- Physical therapy: TENS
- Biofeedback
- Acupuncture
- Trigger point injection
- Botox injection[1]

The use of injections such as trigger point injections, epidurals, and cervical facet injection and botulinum toxin type A remain useful adjuncts in the management of tension-type headache. For patients with localized areas of muscle pain and tenderness, injections may be useful as part of a comprehensive treatment program though recurrent injections may be required.[2]

Conclusion

Tension-type headache is the most common primary headache and has common features of migraine. It may co-exist with migraine and pain diary helps in proper diagnosis of TTH. Tension-type headache has multifactorial aetiology, therefore, both pharmacological and non-pharmacological strategies should be used to treat this condition.

REFERENCES

1. Jensen R, Olesen J. Tension type headache: An update on mechanism and treatment. CurrOpin Neurol. 2000;13:285–89.
2. Yu S, Han X. Update of chronic tension-type headache. Curr Pain Headache Rep.2015;19(1): 469. doi: 10.1007/s11916-014-0469-5.

CHAPTER

16

Migraine

Ravi Shankar Sharma and Abdulkafi Alsaied

INTRODUCTION

Migraine is one of the most common complaints encountered by neurologists in day to day practice.[1] It is an episodic primary headache disorder.[2] Symptoms typically last 4 to 72 h and may be severe. Pain is often unilateral, throbbing, worse with exertion, and accompanied by symptoms such as nausea and sensitivity to light, sound, or odours. Aura occurs in about 15–30% of patients, usually just before but sometimes after the headache.[3]

Epidemiology

Migraine most commonly begins during puberty or young adulthood, growing and fading in frequency and severity over the ensuing years; it often diminishes after the age of 50.[4] Migraine also tends to run in families.

Pathophysiology

The pathophysiology of migraine is very complicated and has many mechanisms which forms the basis of treatment regimes. The pain of migraine is believed to be caused by the vasodilatation of intracranial vasculature. Serotonin and Calcitonin gene related peptide (CGRP) are thought to mediate the pain of migraine by causing vasodilation.[5] It is also hypothesized that a primary neuronal dysfunction may cause stimulation of the trigeminal ganglion and lead to the release of vasoactive neuropeptides (substance P, CGRP and neurokinin A). These mediators cause inflammation of the intracranial vessels and duramater and thereby account for the symptoms. Also, genetic susceptibility plays a role.[6]

Clinical Manifestations[3,4]

Migraine is a disorder of recurrent attacks. The attacks unfold through a cascade of events that occur over the course of several hours to days. A typical migraine attack progresses through four phases: Prodrome, aura, headache and postdrome.

Prodrome

Occurs in up to 60 % of patients and appears 24 to 48 hours prior to the onset of headache. Frequently symptoms include: Euphoria, depression, irritability, food cravings, constipation, neck stiffness, and increased yawning.

Aura

Occurs in up to 25 % of patients and usually precedes the headache. Symptoms usually develop gradually within no longer than one hour, and are completely reversible. Symptoms can be positive or negative.

Positive Symptoms

- Visual (bright lines, shapes, objects),
- Auditory (tinnitus, noises, music),
- Somatosensory (burning, pain, paresthesia),

- Motor (jerking or repetitive rhythmic movements).

Negative symptoms such as loss of vision, hearing, feeling, or ability to move a part of the body.

Types of aura: Auras are most often visual, but can also be sensory, verbal, or motor disturbances.

1. **A visual aura** classically begins as a small area of visual loss often just lateral to the point of visual fixation. It may either appear as a bright spot or as an area of visual loss. Over the following five minutes to one hour, the visual disturbance expands and shape changes. As the aura resolves, vision usually returns first to the areas of central vision initially affected by the aura.
2. **The sensory aura** is also common and typically follows the visual aura within minutes, although it may also occur without the visual aura. A sensory aura usually begins as a tingling sensation in one limb or on one side of the face, then migrates across other side of the face or down the limb. The slow spread of positive symptoms (scintillations or tingling) followed by negative symptoms (scotoma or numbness) is quite characteristic of migraine with aura.
3. **Language or dysphasic aura** is less common and cause transient mild wording difficulties or frank dysphasia with paraphasic errors.
4. **Motor aura** is very rare and cause weakness in the limbs and possibly over the face on one side of the body

The aura symptoms may occur either singly or in sequence and usually develop gradually over more than five minutes. (It must be differentiated from transient ischemic attack (TIA) or stroke which occurs suddenly). Migraine aura without headache also may occur in some patients and again we have to differentiate it from transient ischemic attacks, especially in elderly patients.

Headache

The headache of migraine is often but not always unilateral and tends to have a throbbing or pulsatile quality, especially as the intensity increases. Then patients frequently experience nausea and sometimes vomiting. Many individuals report photophobia or phonophobia during attacks, leading such patients to seek relief by lying down in a dark, quiet room. In addition to other features such as osmophobia and cutaneous allodynia may occur during attacks.

Untreated headache can last from four hours to several days and even longer but many attacks resolve after sleep.

Cutaneous allodynia is the perception of pain produced by innocuous stimulation of normal skin and may result from sensitization of central pain pathways in migraine.

As for example, brushing hair, touching the scalp, shaving, or wearing contact lenses may trigger allodynic symptoms of pain during migraine. Additional symptoms may include soreness, tenderness, or difficulty in resting on the allodynic side.

Severe or persistent cutaneous allodynia may respond to abortive and prophylactic therapy.

Postdrome

When the spontaneous throbbing of the headache resolves, the patient may experience a postdromal phase, during which sudden head movement transiently causes pain in the location of the antecedent headache. During the postdrome, patients often feel drained or exhausted, although some report a feeling of mild elation or euphoria.

Triggers or Precipitating Factors

Common triggers include

- Emotional stress
- OCP and other hormone therapy
- Starvation
- Weather changes
- Sleep disturbances
- Strong odors

- Neck pain
- Flashing lights
- Alcohol
- Smoke
- Certain foods like cheese, chocolate, etc.
- Exercise
- Sexual activity
- Physical exertion

Diagnosis[1,3,7,8]

A detailed history and physical examination usually point to the diagnosis. A positive family history may be an additional clue. The International Classification of Headache Disorders, 3rd edition (ICHD-3), specifies diagnostic criteria for migraine (Fig. 16.1) as given below:

Diagnostic criteria for migraine without aura (ICHD-3)

A. At least five attacks fulfilling criteria B–D
B. Headache attacks lasting 4–72 hours (when untreated or unsuccessfully treated)
C. Headache has at least two of the following four characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
D. During headache at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis.

Diagnostic criteria for migraine with aura (ICHD-3)

A. At least two attacks fulfilling criteria B and C
B. One or more of the following fully reversible aura symptoms:
   1. Visual
   2. Sensory
   3. Speech and/or language
   4. Motor
   5. Brainstem
   6. Retinal
C. At least three of the following six characteristics:
   1. At least one aura symptom spreads gradually over >5 minutes
   2. Two or more aura symptoms occur in succession
   3. Each individual aura symptom lasts 5–60 minutes
   4. At least one aura symptom is unilateral
   5. At least one aura symptom is positive
   6. The aura is accompanied, or followed within 60 minutes, by headache
D. Not better accounted for by another ICHD-3 diagnosis.

Diagnostic criteria for migraine with typical aura (ICHD-3)

A. Attacks fulfilling criteria for Migraine with aura and criterion B below
B. Aura with both of the following:
   1. Fully reversible visual, sensory and/or speech/language symptoms
   2. No motor, brainstem or retinal symptoms.

Variants of migraine: Diagnosis of migraine is mainly clinical, however, certain types of migraine can pose diagnostic difficulties and need special mention.

Hemiplegic Migraine

In this type, aura is characterised by motor weakness which is typically unilateral. Additionally, sensory and visual symptoms may also be present. It may either be sporadic or familial.

Retinal/Ocular Migraine

It is a rare condition characterised by repeated attacks of monocular scotomata or blindness lasting less than one hour, associated with or followed by headache.

Migraine with Brainstem Aura/Basilar Migraine

It is an uncommon form of migraine associated with symptoms of aura originating from the brainstem. The aura may consist of a combination of vertigo, dysarthria, tinnitus, diplopia, ataxia, decreased level of consciousness without associated motor weakness.

Vestibular Migraine/Migrainous Vertigo

It is characterised by episodic vertigo along with headache and other clinical features of migraine.

Menstrual Migraine/Catamenial Migraine

In this type, headache occurs during or at the onset of menstruation. Women with menstrual migraine may also have migraine at other times during the month.

Indication for imaging in cases of migraine: The diagnosis is clinical but neuroimaging may be required in the following situations:

- The "first or worst" headache
- Recent significant change in the pattern, frequency, or severity of headaches
- New or unexplained neurologic symptoms or signs
- Headache always on the same side
- Headaches not responding to management
- New-onset headache after the age of 50 years
- New-onset headache in patients with cancer or HIV infection
- Associated symptoms and signs such as fever, stiff neck, papilledema, cognitive impairment, or personality changes.

Differential Diagnosis[7–9]

Migraine can be confused with other primary headaches like tension type headache and cluster headache. Hemiplegic migraine, migraine with brainstem aura, vestibular migraine and retinal migraine may pose diagnostic difficulties with sinister CNS conditions like stroke, TIA, CNS infections and intracranial SOL. In these cases, an imaging of the brain may provide useful information.

Management [4,10–13]

There is no cure for migraine and prevention is difficult, but treatments can help reduce the number of attacks. Migraines vary greatly from person to person and so does the treatment. The five treatment options available to migraine sufferers include:

- Abortive management
- Preventive management
- Non-pharmacological interventions
- Others

Abortive Management

The basic principle of abortive management is to educate patients about their condition and about the risk of medication overuse and abuse. Eliminate the triggers and advise adequate and specific strong agents for severe headache patients, to them who respond poorly to NSAIDs or combination analgesics. Select a non-oral route of administration because of migraine-induced gastric stasis, nausea and vomiting and also add anti-emetic for such patients. In pregnant women with migraine avoid medicine with adverse fetal effects.

Drugs and other Methods used for Abortive Management

NSAIDs: All NSAIDs may be beneficial in patients of migraine with or without aura.

Serotonin 1B/1D Agonists (Triptans): They inhibit the release of vasoactive peptides and consequently inhibit inflammation and promote vasoconstriction. Various triptans are available but the choice of agent should be individualised. Patients who do not respond to one triptan may respond to the other. However, they should be avoided in hemiplegic migraine and basilar migraine. Contraindications include uncontrolled hypertension, ischemic stroke, ischemic heart disease, prinzmetal angina and pregnancy.

Ergots: Ergotamine and dihydroergotamine alone and in combination with caffeine and other analgesics, have been used for the abortive management of migraine. Dihydroergotamine (DHE 45) is also an alpha-adrenergic blocker and is a weaker arterial vasoconstrictor and more potent venoconstrictor than ergotamine tartrate. DHE 45 has fewer side effects than ergotamine; it does not cause the

development of physical dependence or rebound headaches. They are also available for intravenous, intramuscular, subcutaneous, and intranasal use. Contraindications include hypertension or ischemic heart disease, in combination with MAO inhibitors, and in older adults.

Other Options

Adding **parenteral dexamethasone** to the abortive therapy reduces the rate of early headache recurrence. However, no additional benefit for immediate relief of headache is seen. Long term glucocorticoid therapy has potential risks and should be avoided.

Opioids and barbiturates can be used but are associated with a higher incidence of medication overuse headache.

Transcutaneous magnetic stimulation may prove to be useful as a second-line intervention for those who have episodic migraine with aura that does not respond to first-line therapy with triptans or other agents discussed above or who are unable to take these agents because of contraindications or intolerance. TMS should not be used to treat migraine in patients who have epilepsy, since there is a theoretical concern that TMS could trigger seizures.

General guidelines followed for abortive management

- For mild to moderate migraine attacks not associated with vomiting or severe nausea, simple analgesics (NSAIDs, acetaminophen) or combination analgesics are first choice agents
- For mild to moderate attacks with severe nausea or vomiting, an oral or rectal antiemetic drug can be used in conjunction with simple or combination analgesics.
- For moderate to severe migraine attacks not associated with vomiting or severe nausea, non-oral migraine-specific medications including subcutaneous sumatriptan, nasal sumatriptan and zolmitriptan, non-oral antiemetic agents, and parenteral dihydroergotamine can be used.
- For variable severity migraine attacks associated with vomiting and nausea, give two or more options for self-management, including oral medications for mild to moderate attacks and non-oral medications (e.g. subcutaneous or nasal triptans) for more severe attacks or those associated with vomiting or severe nausea.

Preventive Management

The main goals of preventive management is to reduce attack frequency, severity, and duration. It is also aimed to improve responsiveness of medical management of acute attacks and to prevent progression or transformation of episodic migraine to chronic migraine.

Preventive therapy is indicated when migraine attacks causes significant disability despite appropriate acute management and there is contraindication, failure or serious adverse effects of acute therapies. Preventive migraine therapy is also indicated to reduce the risk of neurologic damage in the presence of uncommon migraine conditions like hemiplegic migraine and migraine with brainstem aura.

Therapeutic lifestyle measures may be beneficial for controlling migraine, including good sleep hygiene, routine meal schedules, regular exercise, and managing migraine triggers. A headache diary is useful for estimating the number and severity of headaches each month and for identifying precipitating factors.

Drugs for Preventive Management

1. **Beta blockers**, particularly metoprolol, propranolol, and timolol, are effective for migraine prevention.
2. **Calcium channel blockers**, angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs) are effective for migraine prevention but less documented than beta blocker.
3. **Serotonin-norepinephrine reuptake**

inhibitor (SNRI) is effective particularly when migraine is accompanied with panic disorder, generalized anxiety disorder, or social anxiety disorder.

4. **The tricyclic antidepressants** most commonly used for migraine prevention.
5. **Anticonvulsants:** Sodium valproate and topiramate which is as effective as propranolol, and may have a modest advantage over valproate.
6. **Gabapentin:** The evidence is insufficient to determine the effectiveness of gabapentin.

Other Suggested Interventions for Preventive Therapy

Acupuncture: Clinical trial evidence suggests that classic acupuncture for migraine headache is more effective than oral pharmacologic placebos, but not more effective than sham needling or traditional medical therapy.

Transcutaneous electrical nerve stimulation (TENS) effectiveness still not proved. But the device used TENS is approved for marketing in the United States, Canada, Europe, and several additional countries.

Surgery: Surgical removal of muscle or nerve tissue from headache "trigger sites" may be an effective management for selected patients with frequent migraine headache.

Conclusion

Migraine is the most common primary headache. It has variable presentation and multifactorial aetiopathology. Migraines are believed to be due to a mixture of environmental and genetic factors. The goal of migraine treatment is to control pain and restore the functional ability. Education of the patients and effective treatment (with drugs and other adjuncts) is the mainstay of successful management.

REFERENCES

1. Ravishankar K. The art of history-taking in a headache patient. *Annals of Indian Academy of Neurology*. 2012;15(Suppl 1):S7–S14. doi:10.4103/0972-2327.99989.
2. Headache classification committee, International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain. Cephalalgia. 2004;24(Suppl 1):1–160. [PubMed]
3. Martin VT. Simplifying the diagnosis of migraine headache. Adv Stud Med. 2004; 4 (4): 200–7.
4. Chawla J. Migraine Headache**.** http://emedicine.medscape.com/article/1142556-overview. Updated: Apr 19, 2016.
5. Cutrer FM, Bajwa ZH. Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. Available at http://www.uptodate.com.
6. GoadsbyPeter J. Pathophysiology of migraine. Ann Indian Acad Neurol. 2012 Aug; 15(Suppl 1): S15–S22.
7. Marks DR, Rapoport AM. Diagnosis of migraine. Seminars in Neurology 1997. 17(4):303–6.
8. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). International Headache Society 2013. Cephalalgia 33(9):629–808.
9. Russell MB. The differential diagnosis and boundaries of migraine. In: Multidisciplinary management of migraine-Pharmacological, Manual and other therapies.Fernández-de-las-Peñas C,Chaitow L, Schoenen J (edt.) 2013; Ch2: pp 11–13. Jones and Bartlett Learning, Burlington, USA.
10. Smith JH, Bajwa ZH. Acute treatment of migraine in adults. Available at http://www.uptodate.com. Last updated**:** Jan 19, 2016.
11. Borghol A, Charles B, Hawawini F. Pharmacologic and complementary therapy for migraine prophylaxis. US Pharm.2013;38:23–6.
12. Smith JH, Bajwa ZH. Preventive treatment of migraine in adults. Available at: http://www.uptodate.com. Last updated**:** Jan 19, 2016.
13. Canadian Headache Society Guideline Acute Drug Therapy for Migraine Headache. The journal (Canadian Journal of Neurological Sciences) 2013; 40:5.

CHAPTER

17

Cervicogenic Headache

Ravi Shankar Sharma, Monika Dabgotra and Debjyoti Dutta

INTRODUCTION

Cervicogenic headache (CEH) is a secondary headache in which the pain generator or source of pain is in the neck. CEH is often unilateral and usually occur on the same side, however, it can become bilateral in due course. It starts in the neck and spreads over head or face on ipsilateral side. Cervical facet dysfunction is probably the most important clinical source for CEH.[1]

Epidemiology

The estimate of the prevalence of cervicogenic headache ranges between 2.5% and 13.8%, however, prevalence is 53% in patients with headache after whiplash. CEH is four times more prevalent in women.

Types of Cervicogenic Headache

Three different cervicogenic headaches can be described according to the area of reference of pain: (a) occipital, (b) occipitotemporomaxillary form and (c) supraorbital form as shown in Fig. 17.1. These forms can exist as mixed types.

Occipital headache: Occipital headache is felt at the occiput and can radiate to the vertex. It corresponds to the territories of the posterior rami of C2 and C3 (Fig. 17.2).

Occipitotemporomaxillary headache: The occipitotemporomaxillary headache is located in the retroauricular, mastoid, and parietal region and radiates toward the inferior maxilla. Pain is found ipsilateral to the facet joint at C2–3.

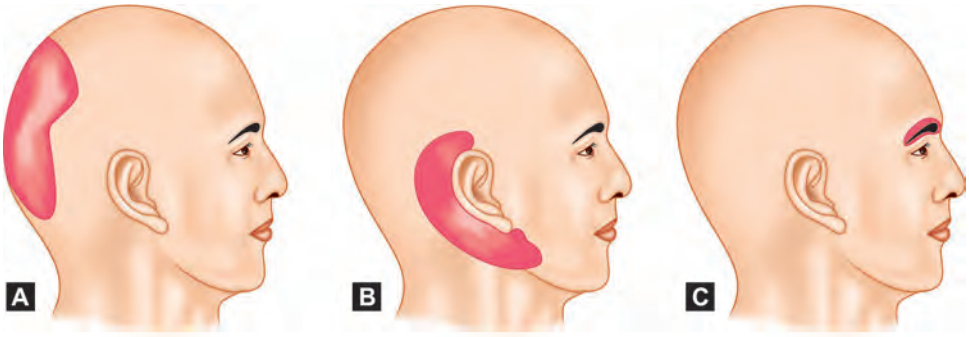


Fig. 17.1: Three types of cervical origin headache (A) Occipital form; (B) occipitotermporomaxillary form; (C) Supraorbital form (most frequent)

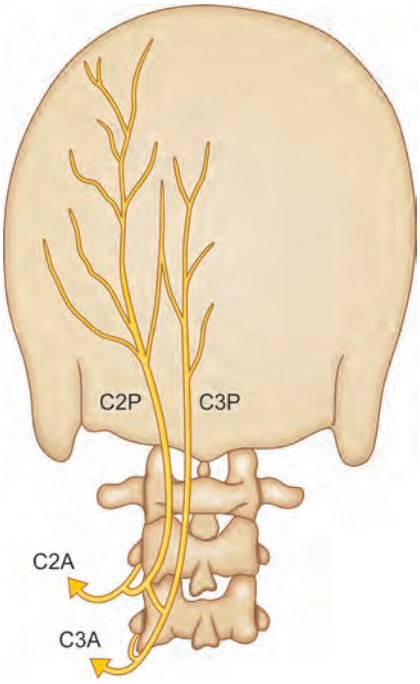


Fig. 17.2: Posterior primary rami of C2 and C3 (C2P and C3P) and anterior primary rami of C2 and C3 (C2A and C3A)

Supraorbital Headache: Supraorbital headache is the most frequent headache of cervical origin. The mechanism for reference of pain to supraorbital area is described above.

Pathophysiology

Repetitive turning or twisting of neck for many hours a day causes strain injury to ligaments and muscles of neck. Chronic strains also result in pathological changes in facet joint and intervertebral disc which results in direct activation and sensitization of nociceptors which carry pain signals. There is increased levels of various neurotransmitters which are responsible for pain. The severity of symptoms depends upon the sum of nociception from cranial and extra-cranial tissues.

Clinical Features

Cervicogenic headache is predominantly unilateral[2] but can be bilateral too. Pain begins in the neck and referred to frontal, temporal or orbital region on the ipsilateral side. The pain perceived in these areas may be maximum than in the neck. Headache is usually deep, non-throbbing or non-pulsating in character, of moderate to severe intensity, and occur in attacks. Duration of attack may range from a few hours to several days. These attacks of headache may be triggered by certain neck movements or sustained, awkward head positioning. There is reduced range of movements in neck with shoulder or arm pain which is non-radicular in nature. Other associated features like nausea, photophobia, phonophobia, dizziness, ipsilateral blurred vision or difficulties on swallowing may also be present.

Physical Examination

There is reduced range of motion in neck and patients may experience tenderness on firm palpation of the upper part of the neck with muscle tightness in this region.

Diagnosis

A comprehensive history and physical examination helps in forming the clinical diagnosis and rules out underlying structural or systemic disease. Various diagnostic criteria are given in Table 17.1. Positive response to a diagnostic/prognostic block with a local anesthetic confirms the diagnosis of CEH. Conventional imaging studies cannot confirm the diagnosis of cervicogenic headache. However, if there are red flag, then further diagnostic tests like MRI or CT should be considered.

Differential Diagnosis

Organic disorders such as a space-occupying lesion in the posterior fossa, sinus thrombosis, arthritis of the cervical spinal column, etc. should be excluded. Other common primary headache syndromes where symptoms may overlap includes

1. Migraine without aura
2. Tension headache

Table 17.1: Diagnostic criteria for cervicogenic headache (A/t ICHD-3)

Diagnostic criteria: (A/T ICHD-3)
A. Any headache fulfilling criterion C
B. Clinical and/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck, known to be able to cause headache.
C. Evidence of causation demonstrated by at least two of the following:
   1. Headache has developed in temporal relation to the onset of the cervical disorder or appearance of the lesion
   2. Headache has significantly improved or resolved in parallel with improvement in or resolution of the cervical disorder or lesion
   3. Cervical range of motion is reduced and headache is made significantly worse by provocative maneuvers.
   4. Headache is abolished following diagnostic blockade of a cervical structure or its nerve supply
D. Not better accounted by another ICHD-3 diagnosis

3. Cluster headache
4. Hemicrania continua
5. Chronic paroxysmal hemicrania (CPH)

Treatment Options

1. Conservative
   a. Medication-simple analgesics like paracetamol, NSAIDs, opioids provide only transient relief in CEH
   b. Physiotherapy
   c. Manual therapy
   d. TENS
2. Interventional
   Interventional treatment is used when conservative treatment is inadequate or patient develops side effects of drugs. Interventional therapy is very effective and relatively safe technique to manage CEH (Table 17.2). There are mainly two groups of interventional therapy:
   a. Local injections
   b. Radiofrequency treatments
   Evidence based algorithm for interventional procedures (Fig. 17.3) helps in decision making while treating a patient with CEH.
3. Surgical treatments

Table 17.2: Summary of evidence for interventional management in cervicogenic headache

Summary of evidence for interventional management in cervicogenic headache	
Technique	*Score*
Injection of nervus occipitalis major with corticosteroid + local anesthetic.	1B+
Injection of atlanto–axial joint with corticosteroid + local anesthetic.	2C–
Radiofrequency treatment of the ramus medialis (medial branch) of the cervical ramus dorsalis.	2B±
Pulsed radiofrequency treatment of the cervical ganglion spinale (DRG) (C2–C3)	0

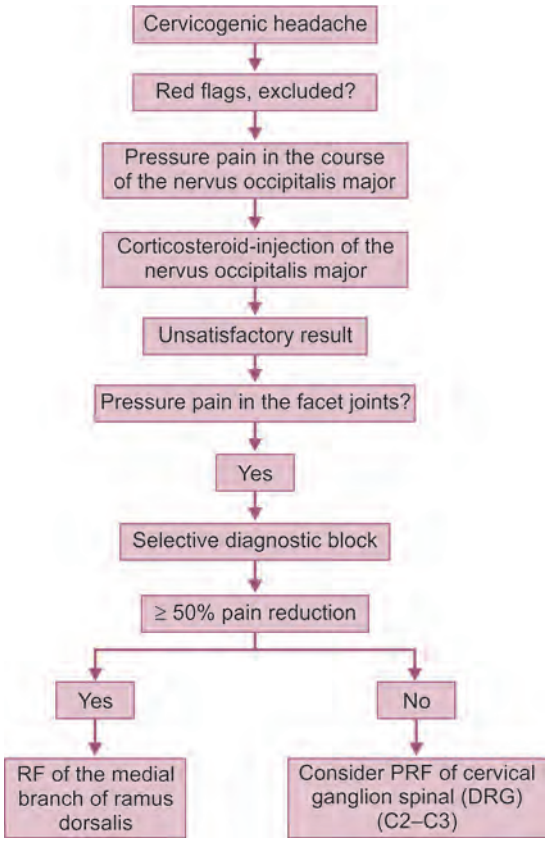

Cervicogenic headache
Red flags, excluded?
Pressure pain in the course of the nervus occipitalis major
Corticosteroid-injection of the nervus occipitalis major
Unsatisfactory result
Pressure pain in the facet joints?
Yes
Selective diagnostic block
≥ 50% pain reduction
Yes
No
RF of the medial branch of ramus dorsalis
Consider PRF of cervical ganglion spinal (DRG) (C2–C3)

Fig. 17.3: Clinical practice algorithm for the treatment of cervicogenic headache[3]

Conclusion

CEH is mainly characterized by unilateral headache symptoms which arises from the neck and radiates to the frontotemporal and possibly to the supraorbital region. Injection of the nervus occipitalis major is recommended after unsatisfactory results with conservative treatments. In the case of an unsatisfactory outcome after injection of the nervus occipitalis major, RF treatment of the medial branch of the cervical ramus dorsalis can be considered. If the result is unsatisfactory, PRF treatment of the ganglion spinale (DRG) of C2 and/or C3 can be considered.

REFERENCES

1. Haldeman S, Dagenais S. Cervicogenic headaches: a critical review. Spine J 2001;1:31–46.
2. Antonaci F., Sjaastad O., Cervicogenic headache: A real headache. Curr Neurol Neurosci Rep, 2011. 11(2): p. 149–55.
3. P. Cervicogenic headaches: An evidence-led approach to clinical management. International Journal of Sports Physical Therapy. 2011;6(3):254–66.

CHAPTER

18

Cluster Headache

Shane Miraj and Ravi Shankar Sharma

Cluster headache[1] is a primary headache disorder,[2] causing one of the most terrible headaches known to mankind. Its usual age of onset is between 30 and 40 years and it is more common in males. In most patients it has a circadian and circannual periodicity suggesting a hypothalamic role in its pathogenesis. Neurological referral is suggested as management can be difficult.

Characteristics

Cluster headache is characterized by:[3]

- Severe or very severe deep boring unilateral orbital or supraorbital pain and/or temporal pain lasting from 15 to 180 min if untreated
- Ipsilateral conjunctival injection and/or lacrimation
- Ipsilateral nasal congestion and/or rhinorrhoea
- Ipsilateral eyelid oedema
- Lacrimation along with conjunctival injection and nasal congestion forms the classic triad
- May be accompanied by a prodrome of vague discomfort around the eye, temple, forehead and neck
- Sometimes, pain can be around maxillary and mandibular region (lower half syndrome)
- Sense of restlessness or agitation
- May rarely be associated with Horner's syndrome and cardiovascular changes and arrhythmias
- May be triggered by alcohol, caffeine, nitroglycerine, exercise, strong odours and elevated temperature

Attacks can vary in frequency from 1–8/day and are limited to the same side in every attack.

Pathophysiology

It is poorly understood and complex. A neurovascular origin of pain is suggested. Probable episodic inflammation of the cavernous sinus resulting in venous congestion and injury to the sympathetic fibres of intracranial internal carotid arteries and its branches is thought to play a role.

Diagnosis

Diagnosis is primarily clinical based on history and normal physical and neurologic examination (Table 18.1). Blood investigations may be normal and ophthalmologic evaluation may be required in patients with significant ocular symptoms. Neuroimaging is indicated only if the presentation is a typical or a sinister cause is suspected.

Differential Diagnosis

Diagnosis is straightforward in typical presentations. However, diagnostic difficulties may be posed in atypical presentations in which cases it can be confused with atypical migraine, trigeminal neuralgia, temporal arteritis among others. In such cases, a neurological referral may be appropriate.

Table 18.1: Diagnostic criteria for cluster headache (ICHD-3)

A. At least five attacks fulfilling criteria B-D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (when untreated).
C. Either or both of the following:
   1. At least one of the following symptoms or signs, ipsilateral to the headache:
      – Conjunctival injection and/or lacrimation
      – Nasal congestion and/or rhinorrhoea
      – Eyelid oedema
      – Forehead and facial sweating
      – Miosis and/or ptosis
   2. A sense of restlessness or agitation
D. Occurring with a frequency between one every other day and 8 per day
E. Not better accounted for by another ICHD-3 diagnosis

Rarely, cluster headache may be caused by a secondary pathology like intracranial SOLs, vascular abnormalities, inflammatory disorders and trauma. In such cases, presentation may be atypical and a neuroimaging may be essential.

Management[4]

Abortive Treatment

Inhaled 100% oxygen delivered using a face mask at a flow rate of 7–8L/min for 15 min provides relief in many patients within 15 minutes.

Sumatriptan when used subcutaneously has very short and rapid onset of action and is effective in symptomatic relief of attacks. Oral form has a longer onset of action and therefore not the first choice. Adverse reactions includes local site reaction, nausea and vomiting and a pressure sensation in the throat and chest. It is contraindicated in patient with ischemic heart disease and uncontrolled hypertension.

Dihydroergotamine (DHE) is available in intranasal and injectable forms. 1 mg IV rapidly aborts the attack. It is contraindicated in patients with coronary or peripheral ischemic disease.

Nasal Lidocaine and nasal Cocaine are amongst the other options that can be used.

Prophylactic Therapy

The purpose of prophylactic therapy is to reduce the frequency, duration and severity of attacks and to interrupt the cycle of cluster headache. It is initiated at the onset of a new cycle simultaneously with symptomatic therapy. The patient should remain on the prophylactic regimen for at least 2 to 4 weeks after the last cluster attack. Discontinuation of treatment should be gradual.

Corticosteroids

They are effective in suppressing attacks at the beginning of a cluster cycle, while the prophylactic therapy is taking effect. 60 to 80 mg of prednisone per day for 2 to 3 days followed by reducing 10 mg every 2 to 3 days. Dexamethasone 8 mg per day for 2 weeks, followed by 4 mg a day for 1 week, may be used as an alternative. Other prophylactic agents should be initiated along with it.

Lithium Carbonate

It is the drug of choice. It is started at a dose of 300–600 mg/day and increased by the end of the fourth week to 600–900 mg/day. It has a narrow therapeutic window. Renal and thyroid functions should be monitored closely. NSAIDs and diuretics if used concomitantly can increase lithium concentrations.

Ergotamine Derivatives

They are useful in recurrent attacks. They should not be used in peripheral vascular disease, coronary artery disease, uncontrolled hypertension, fever, sepsis, pregnancy and within 24 hours of using triptans.

Melatonin, Topiramate, Clonidine and Baclofen can also be used.

Interventional Management

In refractory cases and in patients with contraindications to medical therapy, surgical

interventions can be tried. **Greater occipital nerve blockade, sphenopalatine ganglion blockade and continuous hypothalamic deep brain stimulation** are some of the options that can be tried.

Conclusion

Cluster headache, although a relatively rare headache disorder, has a special place in headache pathophysiology and management. Establishing the diagnosis is facilitated if the physician is cognizant about the disorder. Most patients respond to treatment and if therapy is initiated within the first week of the cycle, the prognosis is excellent. It is especially important for a newly diagnosed patient to understand the origin and natural course of the disorder.

REFERENCES

1. Urban GJ, Diamond S. Cluster headache. In Pain Management, Steven D. Waldman (Edt.) 2nd Edition. Saunders/Elsevier, Philadelphia, 2011; PP 436–52.
2. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders. Available at:http://ihs-classification.org/en/02_klassifikation/02_teil1/03.01.00_cluster.html
3. Schürks, Markus, et al. "Cluster headache: clinical presentation, lifestyle features, and medical treatment." Headache: The Journal of Head and Face Pain 46.8 (2006): 1246–54.
4. Peter JG. Treatment of Cluster Headache. American Headache Society. Available at:http://www.americanheadachesociety.org/assets/1/7/Peter_Goadsby_Treatment_of Cluster_headache. pdf

CHAPTER

19

Myths in Headache

Ashok Jadon and Ravi Shanakr sharma

Myth: Sinusitis is the most common cause for recurrent headaches.

Fact: The International Headache Society (IHS) classification states that chronic sinusitis is not a cause of headache unless it relapses into an acute sinusitis. It is the primary headache disorder mostly migraine, less likely tension and cluster headaches which are the reason of recurrent headache. Nasal congestion which occurs due to the vasodilation of the nasal mucosa can occur in migraine too as also in sinusitis.[1–4]

Myth: There is a close association between high blood pressure and headache.

Fact: Hypertension is the rarest cause of headache. It could be an incidental finding to have both during the clinical examination. Studies however have reported low prevalence of headache in patients who had a high systolic baseline blood pressure. Incidence of headaches is more in female, however, hypertension is more common in males.[5–7]

Myth: Medication overuse is only a problem with special drugs like ergots, triptans or opiates. Medication withdrawal does not work to treat drug overuse problem and medication withdrawal cannot be done effectively on an outpatient basis.

Fact: All these issues related to misuse of the drugs and the treatment of such misuse is not true. First of all, overuse of simple analgesics and non-steroidal anti-inflammatory can also cause chronic headaches.[8] Secondly, the withdrawal treatment does work effectively in majority of the patients[9] and which can successfully be used on outpatient basis.[10]

Myth: Caffeine helps in relieving headache.

Fact: Caffeine causes dilation of the vessels, in acute headaches it helps in relieving pain but if taken in large doses or for recurrent headaches it makes the pain worst.[8]

Myth: Headache does not affect the quality of life.

Fact: Headache affects functional abilities, personal, social as well as professional life thus affecting the quality of life the most.[11–12]

Myth: Stress precipitates migrane

Fact: Migraine can be triggered by any factor that causes vasodilation of the cranial blood-vessels. Stress is one of the factors to precipitate it, however, it can occur even during periods of relaxation, such as on weekends, during holidays.[13–14]

Myth: In migraine headache preventive therapy should be considered for patients whose disability affects their lives considerably.

Fact: New evidence now suggests that earlier, more aggressive preventive measures could benefit many patients.[15] Clinical experience also suggests that prolonged psychosocial impairment in patients with migraine may be less likely with preventive intervention and if longer migraine is left untreated for long

period it becomes more difficult to inhibit attacks even with preventive medications.[15,16]

Myth: We should not consider recurrent headaches seriously.

Fact: Mostly headaches are not life threatening but at times they may have an association with serious neurological disease and may be pointing towards some pathology which requires prompt investigations and treatment.[17]

Myth: Diagnostic intervention like CT/MRI can diagnose migraine easily.

Fact: Diagnostic interventions plays an important role in ruling out any associated pathology which could be a reason for headache. However, the diagnosis of migraine is clinical and according to the diagnostic criteria laid down by International Headache Society.[1–3, 18]

Myth: All migraines are alike

Fact: There are several subtypes of migraine; migraine without aura or with aura, migraine with brainstem aura, sporadic and familial hemiplegic migraine, and retinal migraine, etc.[18,19]

Myth: Migraine runs in families.

Fact: Migraine have got a genetic basis but it does not mean that if either of the parents have got migraine, then children are also going to be affected.[20]

Myth: Severe recurrent headaches must be migraine and recurrent headaches are a female disorder.

Fact: There are many different types of headaches which are similar or rather more severe in nature than migraine.Cluster headache is one example which is one of the most terrible headaches known to mankind and it is more common in males.[21]

Myth: It is not worth to visit a physician for headache.

Fact: Each year the average headache sufferer loses time and income due to headache disability; these loses exceed the cost of quality medical treatment.[11,12]

Myth: There is no good treatment for migraine.

Fact: After having made a clinical diagnosis of migraine and after taking a proper clinical history, there are lots of therapies to treat migraine successfully. For diagnosis, detailed history and headache diary helps to identify triggers which are responsible for migraine. [22, 23]

Myth: If you do not see flashing lights, then you are not having migraine.

Fact: Seeing flashing lights is a type of aura and only about one-third of patients of migraine have an aura. There are other variants of migraine where aura is absent.[23]

Myth: Migraine is seen in adults.

Fact: Migraine can occur at any age including children. However, it is more prevalent in adults before 50 years and after that again incidence decreases.[23, 24]

Myth: Migraine is more common in women.

Fact: Before adolescence the incidence is equal among males and females. After adolescence 18 percent of women and 8 percent of men have migraines.[23, 24]

Myth: Migraine attacks are for a few hours and do not last more than a day.

Fact: Migraines may last for a few hours (4 to 72 hours) or longer for days, weeks, or even months.[23, 24]

Myth: Only certain types of people get migraines.

Fact: Migraine has no relation with type or personality of people. Researchers have proved that migraine is a genetic and neurological disease.[25]

Myth: Migraines are not life-threatening.

Fact: A migraine itself may not be life-threatening, but complications of migraine and risk factors associated with migraine can be. In rare cases infarction can occur during migraine with aura.[26] Research has confirmed links between migraine and stroke and other cardiovascular diseases. [27]

REFERENCES

1. Jones N. Sinuses headaches: avoiding over and mis-diagnosis. Expert Rev. Neurother. 2009; 9: 439–44.
2. Schreiber CP, Hutchinson S, Webster CJ, Ames M, Richardson MS, Powers C. Prevalence of Migraine in Patients with a History of Self-reported or Physician-Diagnosed "Sinus" Headache. *Arch Intern Med.* 2004; 164(16):1769–72.
3. Kaymakci M,Cikriklar HI, Pay G. The aetiology underlying sinus headaches. Journal of International Medical Research, February 2013 vol. 41 no. 1218–23.
4. ForoughipourM, Sharifian SMR, Shoeibi A, Barabad NE, Bakhshaee M. Causes of headache in patients with a primary diagnosis of sinus headache. Eur. Arch. Otorhinolaryngol. 2011; 268:1593–6.
5. Friedman D. Headache and hypertension: refuting the myth. J Neurol Neurosurg Psychiatry 2002; 72:431.
6. Hagen K, Strovmer LJ, Vatten L, et al. Blood-pressure and risk of headache: a retrospective study of 22,685 adults in Norway. J Neurol Neurosurg Psychiatry 2002;72:463–6.
7. Hagen K, Zwart JA, Vatten L, et al. Prevalence of migraine and non-migrainous headache: head-HUNT, a large population study. Cephalalgia 2000; 30:900–6.
8. Meskunas CA, Tepper SJ, Rapoport AM, et al. Medications associated with probable medication overuse headache reported in a tertiary care headache centre over a 15-year period. Headache 2006; 46:766–72.
9. Zeeberg P, Olesen J, Jensen R. Probable medication overuse headache: the effect of a two-month withdrawal period. Neurology 2006;66:1894–88. 8.
10. Rossi P, Di Lorenzo C, Faroni J, et al. Advice alone vs. structured detoxification programmes for medication overuse headache: a prospective, randomised, open-label trial in transformed migraine patients with low medical needs. Cephalalgia 2006;26:1097–105.
11. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache. 2001;41:646–57.
12. Terwindt GM, Ferrari MD, Tijhuis M, et al. The impact of migraine on quality of life in the general population: the GEM study. Neurology. 2000; 55:624–9.
13. Capobianco DJ, Cheshire WP, Campbell JK. An overview of the diagnosis and pharmacologic treatment of migraine. Mayo Clin Proc. 1996;71:1055–66.
14. Spierings, E. L.H., Ranke, A. H. and Honkoop, P. C., Precipitating and Aggravating Factors of Migraine Versus Tension-type Headache. Headache: The Journal of Head and Face Pain, 2001;41: 554–8.
15. Loder E, Biondi D. General principles of migraine management: the changing role of prevention. Headache. 2005;45(suppl 1):S33–47.
16. Bigal ME, Lipton RB. When migraine progresses: transformed or chronic migraine. Expert Rev Neurother. 2006;6:297–306.
17. Headache Hope Through Research. National Institute of Neurological Disorders and Stroke. National Institutes of Health. Publication date October 2009. Available at: http://www.ninds.nih.gov/disorders/headache/detail_headache.htm. Last Modified November 3, 2015
18. Headache classification committee, International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain. Cephalalgia. 2004;24(Suppl 1) :1–160.
19. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). International Headache Society. Cephalalgia 2013;33(9) 629–808.
20. Goadsby Peter J. Pathophysiology of migraine. Ann Indian Acad Neurol. 2012 Aug; 15(Suppl 1): S15–S22.
21. Urban GJ, Diamond S.Cluster headache. In Pain Management, Steven D. Waldman (Edt.) 2nd Edition. Saunders/Elsevier, Philadelphia, 2011;PP 436–52.
22. Borghol A, Charles B, Hawawini F. Pharmacologic and complementary therapy for migrane prophylaxis. US Pharm.2013;38:23–6.
23. Martin VT. Simplifying the diagnosis of migraine headache. Adv Stud Med. 2004; 4 (4): 200–7.

24. Chawla J. Migraine Headache. http://emedicine.medscape.com/article/1142556-overview. Updated: Apr 19, 2016.
25. Cutrer FM, Bajwa ZH. Pathophysiology, clinical manifestations, and diagnosis of migraine in adults. Available at http://www.uptodate.com.
26. Tietjen GE. Migraine and ischaemic heart disease and stroke: potential mechanisms and treatment implications. Cephalalgia 2007; 27:981–7.
27. Etminan M, Takkouche B, Isorna FC, Samii A. Risk of ischemic stroke in people with migraine: systematic review and meta-analysis of observational studies. BMJ 2005;330:63–5.

v

SECTION

V

Joint Pain Management

Praneet Singh, Rammurthy and R Gurumoorthi (Section Editors)

20. Rheumatoid Arthritis
21. Spondyloarthropathies
22. Shoulder Pain
23. Knee Pain
24. Nonpharmacological Management of Joint Pain
25. Management of Joint Pain
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CHAPTER

20

Rheumatoid Arthritis

Samarjit Dey

Rheumatoid arthritis (RA) is a chronic disabling inflammatory arthritis which has a wide spectrum of disease manifestations. It leads to progressive joint destruction and extra-articular manifestations which account for the disability and increased mortality. Its early recognition and intervention with disease-modifying therapy is very important in preventing the progressive disability. RA most typically presents as polyarticular disease with a gradual onset, but some patients can present with acute onset with intermittent or migratory joint involvement or with monoarticular disease.

Demography

RA is three times more common in females than male and prevalence increases with age with diminishing gender difference. The onset is most frequent during the fourth and fifth decades of life, with 80% of all patients developing the disease between the ages of 35 and 50.[1]

Pathogenesis

Basic pathology is immune response to genetically acquired antigen which leads to antibody production which cross reacts with host tissue. The main gene is linked to HLA DR1&4. It is responsible for 60% of disease incidence. Remaining is related to infection, smoking and life style. Usually synovial tissue is involved which leads to joint destruction and deformities.

Clinical Features

The objectives of clinical assessment for RA are mainly to: (a) establish the diagnosis (b) evaluate the disease activity (c) assess the disease severity (amount of damage and disability) and (d) look for extra-articular manifestations.[2] Usually it is insidious in onset and very rarely around 10%, it can present as acute onset. It starts with prodromal symptoms like fatigue, anorexia, generalized weakness, and vague musculoskeletal symptoms[1] which are then followed by synovitis. Classically it involves multiple joints in symmetrical fashion. Sometime it can involve single joint also. Patients usually will complaint about pain and stiffness (early morning stiffness lasting more than 60 minutes) in involved joints.

Most commonly proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints of the hands, wrists, and small joints of the feet including the metatarsophalangeal (MTP) joints are involved. In some cases large joints like shoulders, elbows, knees, and ankles can also be affected. Clinical diagnosis can be easier when small joints are involved. The distal interphalangeal (DIP) joints and spine (except cervical spine) are generally spared.[3]

On examination of joint, there will boggy swelling due to synovitis, sometimes warmth, restricted range of movements and more pain on active movement than passive movement of joint. Permanent deformities like Boutonniere deformity, Swan-neck deformity and

Claw toe deformity can be seen in late stages. Extra-articular manifestations[2] (Table 20.1) like rheumatoid nodules, vasculitis, interstitial lung disease, scleritis, episcleritis, etc. has to be noted. There are certain manifestation which needs aggressive treatment which are termed red flags[2] (Table 20.2) and those patient should be referred immediately to higher speciality centres.

Table 20.1: Extra-articular manifestation of rheumatoid arthritis

Specific organ	*Clinical manifestations*
Haematological	• Anemia • Neutrophilia • Thrombocytosis • Felty's syndrome
Cutaneous	• Rheumatoid nodules • Peripheral vasculitis • Leg ulcers • Alopecia
Neurological	• Entrapment neuropathies such as carpal tunnel syndrome • Mononeurits multiplex • Peripheral neuropathies
Ocular	• Xerophthalmia • Scleritis • Episcleritis
Pulmonary	• Pleural effusions • Interstitial lung disease • Bronchiolitis oblitrans
Cardiac	• Pericarditis • Coronary vasculitis (rare)
Others	• Dry mouth • Osteoporosis • Muscle wasting

Table 20.2: Red flags in rheumatoid arthritis

Red flags	*Reason*
Atlantoaxial dislocation	Can cause spinal cord compression
Amyloidosis	Needs renal support
Monoarticular flare	To rule out septic arthritis
Pericarditis	Needs urgent steroid treatment and cardiac support
Eye involvement	Long standing can lead to perforation

Laboratory Evidence

Baseline complete blood count is done which can show variable results like anemia, neutrophilia and thrombocytosis. Elevated inflammatory marker like erythrocyte sedimentation rate, C-reactive protein and serum ferritin can be elevated in active disease. Rheumatoid factor [RA], IgM antibody against Fc portion of IgG antibody is usually done as primary test in rheumatoid arthritis. It is not only elevated in RA but also elevated in other conditions which include systemic lupus erythematosus, Sjögren's syndrome, chronic liver disease, sarcoidosis, interstitial pulmonary fibrosis, infectious mononucleosis, hepatitis B, tuberculosis, leprosy, syphilis, subacute bacterial endocarditis, visceral leishmaniasis, schistosomiasis, and malaria.[1] The presence of rheumatoid factor does not establish the diagnosis of RA, and hence it is not useful as a screening procedure. However, it has prognostic significance because patients with high titers tend to have more severe and progressive disease with extra-articular manifestations like rheumatoid nodules, vasculitis etc. Anti-cyclic citrullinated peptide [Anti-CCP] antibody test has a similar sensitivity and a better specificity for RA than rheumatoid factor, 82% vs 95% and, therefore it is more preferred.[2]

Radiographic Evidence

Specific finding in radiographic image is not diagnostic for RA. But some features like symmetrical periarticular lesions are characteristic for RA. Juxta-articular osteopenia may become apparent within weeks of onset followed in months with loss of articular cartilage and bone erosions. Radiography gives idea about extent of cartilage destruction and bone erosion produced by the disease, particularly when one is attempting to estimate the aggressive nature of the disease, monitoring the impact of therapy with disease-modifying drugs, or determining the need for surgical intervention.[1] Computed tomography chest can give an idea about pleural effusion and interstitial lung disease.

Diagnostic Criteria

As there is constellation of symptoms, signs and investigations, diagnosis of RA is based on criteria and their scores. The 2010 American College of Rheumatology/European League[4] against Rheumatism classification criteria (Table 20.3) for rheumatoid arthritis are followed at present. In the new classification criteria for RA (score-based algorithm) score of categories A–D to be added; a score of 6/10 is needed for classification of a patient as having definite RA. Although patients with a score of 6/10 are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.

Table 20.3: The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

To be applied to patients (1) who have[3] 1 joint with definite synovitis, excluding the DIP joints, first MTP joints, and first CMC joints, and (2) in whom the synovitis cannot be explained by another disease.

Criteria	*Score*
A. Joint involvement:	
1 large joint	0
2–10 large joints[a]	1
1–3 small joints (with or without involvement of large joint)	2
4–10 small joints (with or without involvement of large joint)	3
> 10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification):	
Negative RF and negative anti-CCP antibodies	0
Low-positive RF or low-positive anti-CCP antibodies[c]	2
High-positive RF or low-positive anti-CCP antibodies[d]	3
C. Acute phase reactants:	
Normal CRP level and normal ESR	0
Abnormal CRP level or abnormal ESR	1
D. Duration of symptoms:	
<6 weeks	0
≥6 weeks	1

ACR, American College of Rheumatology; European League Against Rheumatism; RA, rheumatioid arthritis; DIP, distal interphalangeal; MTP, metatarsophalangeal; CMC, carpometacarpal; MCP, metacarpophalangeal; PIP, proximal interphalangeal; IP, interphalangeal; RF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated protein; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

[a]Large joints = shoulders, elbows, hips, knees, ankles.

[b]small joints = MCPs, PIPs, second-fifth MTPs, thumb IPs, wrists.

[c]Low-positive is ≤ 3 times the upper limit of normal.

[d]High-positive is > 3 times the upper limit of normal.

Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement. When there is involvement of more than 10 joints, at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g. temporomandibular, acromioclavicular, sternoclavicular, etc.).

Treatment

The goals of therapy for RA include relief of pain, reduction of inflammation, protection of articular structures, maintenance of function, and control of systemic involvement.[1] Treatment as such is totally palliative. For symptomatic control of disease, non-steroidal anti-inflammatory drugs [NSAIDs], simple analgesics and steroids [low dose 7.5 mg/day] are used. Considering side effect profile of NSAIDs like gastrointestinal, renal, pulmonary and cardiac damage, cyclooxygenase [COX]-2, inhibitors are used. But unfortunately due to sudden cardiac events in COX-2 inhibitors, nowadays lot of drugs are withdrawn from market.

Third line of drug belongs to disease modifying anti-rheumatic drugs [DMARDs]. These agents include methotrexate, sulfasalazine, hydroxychloroquine, gold salts and D-penicillamine. Nowadays it had been recommended to start with high dose for rapid control of disease and then tapered slowly. Methotrexate is the anchor drug in RA treatment and is usually given as 7.5–25 mg

weekly as oral or intramuscular form in order to avoid gastrointestinal side effects. Common side effects include stomatitis, nausea, diarrhea, hair loss. Supplementation with folic acid (1 to 2 mg) can reduce such side effects without significantly reducing efficacy. Bone marrow suppression is uncommon but may occur at low doses in elderly patients. The risk of liver toxicity is increased by alcohol consumption, preexisting liver disease, and possibly by diabetes and obesity. Liver function tests and blood counts are checked every month until the dose is stable and every 2 to 3 months thereafter. It has onset of action early than other drugs but maximum effect occurs after 6 months. Other drugs like sulfasalazine can be used in mild form of disease. Sulfasalazine should be started at 500 mg twice daily and gradually increased to 2 to 3 g daily in divided doses. Monitoring for neutropenia and hepatotoxicity should be performed every 1 to 3 months Chloroquine[2] can be used as add-on drug to other DMARDs. Patient has to take minimum of 8 weeks of a particular drug to consider its efficacy.

When disease is not controlled of DMARDs then biologics are used which include TNF-neutralizing agents (infliximab, etanercept, and adalimumab), IL-1 neutralizing agents (anakinra), those that deplete B cells (rituximab), and those that interfere with T cell activation (abatacept). These drugs should be administered preferably by rheumatologist who has more experience with these drugs as they have more side effect profiles. Then last group of drugs, immunosuppressive and cytotoxic drugs, including leflunomide, cyclosporine, azathioprine, and cyclophosphamide are used when all drugs fails.[1]

Newer Anti-rheumatic Drugs

Iguratimod: is a novel synthetic disease modified anti-rheumatic drug used along other DMARDs like methotrexate. It is used as 25mg orally daily for 4 weeks and the 50 mg daily. It has additional analgesic property which is beneficial in these types of patients.

JAK inhibitors: Janus kinase inhibitors are newer called DMARDs. Three JAK inhibitors, baricitinib, tofacitinib, and upadacitinib, are US FDA approved drugs to treat rheumatoid arthritis.

REFERENCES

1. Peter EL. Rheumatoid arthritis. In: Anthony SF, editor. Harrison's rheumatology. New York: McGraw-Hill; 2010. P. 82–99.
2. Kamran H, Mohammed A. Rheumatoid Arthritis: Clinical Features and Diagnosis. In: Ade Adebajo, editor. ABC of Rheumatoloy. West Sussex: Wiley Blackwell; 2010. P. 71–5.
3. Gary SF. Clinical features of rheumatoid arthritis. Gary SF, Ralph B, Sherine EG, James R, Iain BM, editors. Kelleys Textbook of Rheumatology. Philadelphia: Elsevier saunders;2013. P. 1109 – 36.
4. Daniel A, Tuhina N, Alan JS, Julia F, David TF, Clifton OB, et al. 2010. Rheumatoid Arthritis Classification Criteria. Arthritis and Rheumatism.2010 Sep; 62(9): 2569–81.

CHAPTER

21

Spondyloarthropathies

Samarjit Dey

The spondyloarthropathies are a diverse group of inflammatory arthritides that share certain genetic predisposing factors and clinical features[1] (Table 21.1).[1–3] Their most characteristic feature is inflammatory back pain.[4] Enthesitis, another characteristic feature, involves inflammation at sites where tendons, ligaments, or joint capsules attach to bone. Enthesitis is believed to be the primary lesion in the spondyloarthropathies, whereas synovitis is the main lesion in rheumatoid arthritis. Dactylitis (inflammation of an entire digit), commonly termed "sausage digit," also occurs in the spondyloarthropathies and is thought to arise from joint and tenosynovial inflammation.These disorders include ankylosing spondylitis, reactive arthritis, psoriatic arthritis and spondylitis, enteropathic arthritis and spondylitis, juvenile-onset spondyloarthritis, and undifferentiated spondyloarthritis. Clinical features of common spondyloarthropathy are listed in Table 21.1.

Table 21.1: Clinical features of common spondyloarthropathies

Features	*Ankylosing*	*Reactive arthritis (including Reiter's syndrome)*	*Psoriatic arthritis*	*IBD-associated spondyloarthropathy*
Prevalence	0.1% to 0.2%	0.1%	0.2% to 0.4%	Rare
Age at onset	Late teens to early adulthood	Late teens to early adulthood	35 to 45 years	Any age
Male-to-female ratio	3:1	5:1	1:1	1:1
HLA-B27	90 to 95%	80%	40%	30%
Sarcoilitis				
Frequency	100%	40 to 60%	40%	20%
Distribution	Symmetric	Asymmetric	Asymmetric	Symmetric
Syndesmophytes	Delicate, marginal	Bulky, nonmarginal	Bulky, nonmarginal	Delicate, marginal
Peripheral arthritis				
Frequency	Occasional	Common	Common	Common
Distribution	Asymmetric, lower limbs	Asymmetric, lower limbs	Asymmetric, any joint	Asymmetric, lower limbs

Contd.

Table 21.1: Clinical features of common spondyloarthropathies (Contd.)

Features	*Ankylosing spondylitis*	*Reactive arthritis (including Reiter's syndrome)*	*Psoriatic arthritis*	*IBD-associated spondyloarthropathy*
Enthesitis	Common	Very common	Very common	Occasional
Dactylitis	Uncommon	Common	Common	Uncommon
Skin lesions	None	Circinate balanitis, keratoderma blennorrhagicum	Psoriasis	Erythema nodosum, pyoderma gangrenosum
Nail changes	None	Onycholysis	Pitting, onycholysis	Clubbing
Ocular conditions	Acute anterior uveitis	Acute anterior liveitis, conjunctivitis	Chronic uveitis	Chronic uveitis
Oral conditions	Ulcers	Ulcers	Ulcers	Ulcers
Cardiac conditions	Aorthic regurgitation	Aortic regurgitation, conduction defects	Aortic regurgitation, conduction defects	Aortic regurgitation
Pulmonary features	Upper lobe fibrosis	None	None	None
Gastrointestinal conditions	None	Diarrhea	None	None
Renal conditions	Amyloidosis, lgA nephropathy	Amyloidosis	Amyloidosis	Nephrolithiasis
Genitourinary conditions	Prostatitis	Urethritis, cervicitis	None	None

Investigation

Investigation is done to confirm diagnosis and assess severity of disease.

- Complete blood count, erythrocyte sedimentation rate, c-reactive protein is done to check active inflammatory process.
- In case of suspected ankylosing spondylitis, HLA typing usually HLA B-27 is done. The prevalence of HLA-B27 within patient populations with SpA ranges 50% to 95%.
- SpAs occur in about 2% of the general population and in just over 10% of HLA-B27 positive individuals.
- X-ray and MRI of spine is done to confirm sacroilitis and other features like facet joint inflammation, syndesmophytes, etc. In case of peripheral joint, grading of cartilage and bony destruction can be assessed.
- In case of joint effusion, fluid tap is done to differentiate from infective pathology.
- Scintigraphy can show increased radiotracer uptake in inflamed joints.
- A serum uric acid and urate crystal in joint fluid is done to confirm gouty arthritis.
- Colonoscopy can be done in case of suspected bowel related spondyloarthropathy.

Diagnostic Criteria

As there is no specific sign and investigation A thorough history will elicit symptoms of inflammatory back pain such as morning stiffness, improvement of pain with activity and worsening with rest, and insidious onset. Alternating buttock pain may be present available to confirm spondyloarthropathy, certain criteria are made to confirm different

Table 21.2: Inflammatory back pain criteria set and mnemonic for assessment of spondyloarthritis international society criteria

Calin's criteria	*Berlin criteria for IBP*	*ASAS IBP criteria mnemonic for criteria iPAIN*
Age at onset < 40 yr	Morning stiffness of >30 min duration	Insidious onset
Duration of back pain >3 mo	Improvement in back pain with exercise but not with rest	Pain at night (with improvement upon getting up)
Insidious onset		
Morning stiffness	Nocturnal awakening (second-half of the night only)	Age at onset < 40 yr
Improvement with exercise	Alternating buttock pain	Improvement with exercise
Requires the presence of four of five criteria	The sensitivity is 70%, specificity 81% if two of the four criteria are fulfilled	The sensitivity is 77.0% and specificity 91.7% if at least four out of five criteria are fulfilled

IBP: Inflammatory back pain; ASAS: Assessment of spondyloarthritis international society; iPAIN: Inflammatory PAIN.

types of spondyloarthropathy. In this section all recent classification criteria for spondyloarthritis are listed, starting with inflammatory back pain criteria sets and mnemonic for assessment of spondyloarthritis international society criteria[1] (Table 21.2), 1984 modified New York criteria for ankylosing spondylitis[2] (Table 21.3), Amor criteria[3] (Table 21. 4) and the European Spondyloarthropathy Study Group (ESSG) criteria[4] (Table 21.5) for spondyloarthritis, which cover the whole

Table 21.3: Modified New York criteria for ankylosing spondylitis (1984)

- Clinical criteria:
  - Low back pain and stiffness for more than 3 months that improves with exercise, but is not relieved by rest.
  - Limitation of motion of the lumbar spine in the sagittal and frontal planes.
  - Limitation of chest expansion relative to normal values correlated for age and sex.
- Radiological criterion:
  - Sacroilitis grade ≥ 2 bilaterally or grade 3–4 unilaterally.

Definite AS if the radiological criterion is associated with at least one clinical criterion

Table 21.4: Amor criteria

Clinical symptoms or history of scoring	*Points*
Lumbar or dorsal pain at night or morning stiffness of lumbar or dorsal pain	1
Asymmetrical oligoarthritis	2
Buttock pain	1
If alternate buttock pain	2
Sausage like toe or digit	2
Heel pain or other well-defined enthesopathy	2
Iritis	1
Nongonococcal urethritis or cervicitis within 1 month before the onset of arthritis	1
Acute diarrhea within one month before the 1 mo onset of arthritis	1
Psoriasis, balanitis, or inflammatory bowel disease (ulcerative colitis or Crohn's disease)	2
Radiological findings Sacroilitis (bilateral grade 2 or unilateral grade 3)	3
Genetic background Presence of HLA-B27 and/or family history of ankylosing spondylitis, reactive	2

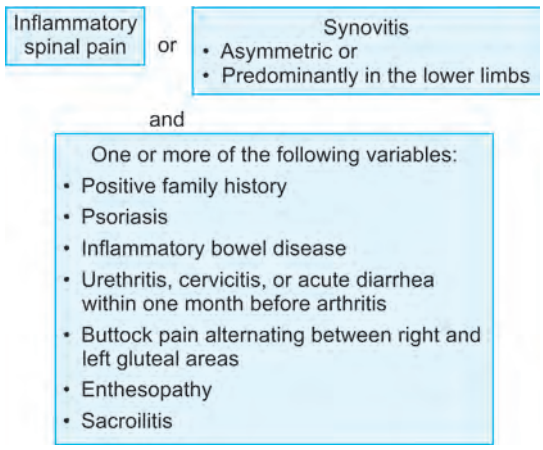
Contd.

Table 21.4: Amor criteria (Cond.)

Clinical symptoms or history of scoring	*Points*
arthritis, uveitis, psoriasis, or inflammatory bowel disease	
Response to treatment Clear-cut improvement within 48h after NSAIDs intake or rapid relapse of the pain after their discontinuation	2
A patient is considered as suffering from spondyloarthropathy if the sum is ≥ 6	

NSAID: Nonsteroidal anti-inflammatory drug; HLA: Human leukocyte antigen.

Table 21.5: European Spondyloarthropathy Study Group (ESSG) criteria


Inflammatory spinal pain
or
Synovitis
• Asymmetric or
• Predominantly in the lower limbs
and
One or more of the following variables:
• Positive family history
• Psoriasis
• Inflammatory bowel disease
• Urethritis, cervicitis, or acute diarrhea within one month before arthritis
• Buttock pain alternating between right and left gluteal areas
• Enthesopathy
• Sacroilitis

spectrum of SpA including axial SpA[5] (Table 21.6) and peripheral SpA[6] (Table 21.7) and psoriatic arthritis study group criteria for the classification of psoriatic arthritis[7] (Table 21.8). The most recent ASAS classification criteria for axial spondyloarthritis were developed for early and established cases and include the MRI technique (active inflammation) as an important tool for early diagnosis. SpA occurs in only approximately 10% of HLA-B27 individuals, the positive predictive value for disease is relatively low. Thus, HLA-B27 testing is generally not clinically useful by itself.

Table 21.6: ASAS criteria for classification of axial spondyloarthritis (to be applied in patients with chronic back pain and age at onset of back pain, 45 years)

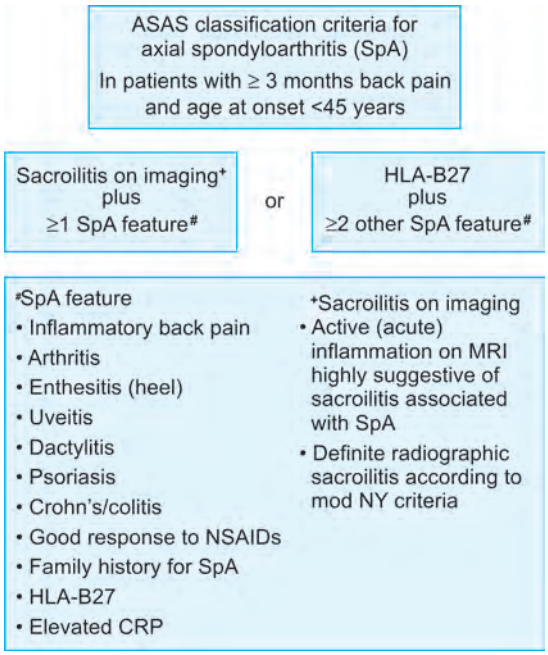

ASAS classification criteria for axial spondyloarthritis (SpA)
In patients with ≥ 3 months back pain and age at onset <45 years
Sacroilitis on imaging⁺ plus ≥1 SpA feature#
or
HLA-B27 plus ≥2 other SpA feature#
#SpA feature
• Inflammatory back pain
• Arthritis
• Enthesitis (heel)
• Uveitis
• Dactylitis
• Psoriasis
• Crohn's/colitis
• Good response to NSAIDs
• Family history for SpA
• HLA-B27
• Elevated CRP
⁺Sacroilitis on imaging
• Active (acute) inflammation on MRI highly suggestive of sacroilitis associated with SpA
• Definite radiographic sacroilitis according to mod NY criteria

Table 21.7: Assessment in spondyloarthritis international society classification criteria for peripheral spondyloarthritis or spondyloarthritis in general

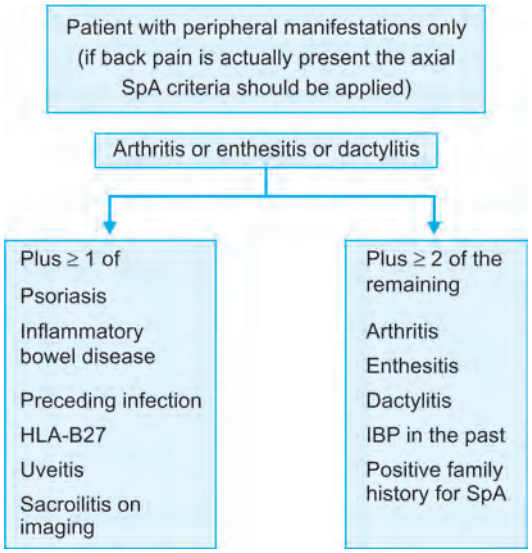


Table 21.8: Classification of psoriatic arthritis study group criteria for the classification of psoriatic arthritis

Inflammatory articular disease (joint, spine or enthesal) and 3 points of following criteria
Evidence of current psoriasis,[1] a personal history of psoriasis, or a family history of psoriasis
Current psoriasis is defined as psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist
A personal history of psoriasis is defined as a history of psoriasis that may be obtained from a patient, family physician, dermatologist, rheumatologist, or other qualified health care provider
A family history of psoriasis is defined as a history of psoriasis in a first-or second-degree relative according to patient report
Typical psoriatic nail dystrophy including anycholysis, pitting, and hyperkeratosis observed on current physical examination
A negative test result for the presence of rheumatoid factor by any method except latex but preferably by enzyme-linked immunosorbent assay or nephelometry, according to the local laboratory reference range
Either current dactylitis, defined as swelling of an entire digit, or a history of dactylitis recorded by a rheumatologist
Radiographic evidence of juxta-articular new bone formation, appearing as ill-defined assification near joint margins (but excluding osteophyte formation) on plain radiographs of the hand or foot

Treatment

The goals of treatment are to relieve symptoms, improve function and delay or prevent structural damage. To some extent treatment of spinal inflammation differs from that of peripheral joint synovitis and enthesitis, so treatment must be tailored to the actual problems in the individual patient at the time.[8] In case of sacroilitis and spondylitis, NSAIDs, COX-2 inhibitiors form first line of drug but long term usage will have renal and gastric damages. Oral and intramuscular steroids form second line drug. Intra-articular injection of steroid can be also tried when oral drug is not tolerated. Tumor necrosis factor [TNF] antagonist forms third line drug and immunosuppressant as last drug. Rehabilitation should be done along with medical treatment. In case of peripheral joints and enthesitis, analgesics like NSAIDs, COX-2 inhibitors and steroid form first line drug. DMARDs forms second line drug followed by TNF anatagonist and immunosuppressant. Oral disease-modifying antirheumatic drugs (DMARDs) have limited efficacy in axial SpA, although methotrexate, sulfasalazine, leflunomide, and azathioprine have been used. There are conflicting data on the efficacy of these agents.[9] In case of gouty arthritis, drugs like allopurinol, febuxostat, and probenecid are used to lower uric acid level below 6 mg/dl.

REFERENCES

1. Ozgur A, Salih O. Classification criteria for spondyloarthropathies. World J Orthop. 2011 Dec; 2(12): 107–15.
2. Vander LS, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York

criteria. Arthritis Rheum. 1984 Apr; 27(4): 361–8.
3. Amor B, Dougados M, Mijiyawa M. Criteria of the classification of spondyloarthropathies. *Rev. Rhum. Mal. Osteoartic.1990;*57:85–9.
4. Dougados, M. et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum. 1991; 34: 1218–27.
5. Rudwaleit, M. et al. The development of Assessment of spondyloarthritis International Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis.2009;68:777–83.
6. Rudwaleit, M. et al. The Assessment of Spondylo arthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann. Rheum. Dis. 2011;70: 25–31.
7. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum. 2006;54:2665–73.
8. Andrew K, Robert I. Spondyloarthritides. In: Ade A, editor. ABC of rheumatology. West Sussex: wiley Blackwell; 2010.p. 79–84.
9. Kabasakal Y, Kitapcioglu G, Yargucu F, et al. Efficacy of SLZ and MTX (alone or combination) on the treatment of active sacroiliitis in early AS. Rheumatol Int. 2009;29:1523–1527.

CHAPTER

22

Shoulder Pain

Kanchan Sharma

Shoulder pain is more common due to multiple pain generators in and around shoulder joint which can be damaged due to high range of moti on, direct injury or by weight transduction across joint and involvement of joint in systemic disease like inflammatory arthropathy, diabetic mellitus, etc. In some cases, pain may be referred from cervical region, diaphragm and myocardial ischemia.

Anatomy of Shoulder Girdle

The shoulder girdle connects the upper limb to the axial skeleton. It consists of acromioclavicular joint (joint between acromion of scapula and clavicle) and shoulder joint (joint between glenoid cavity of scapula and humerus head). Other end of clavicle articulates with the sternum at the sternoclavicular joint.

Shoulder Joint

It is a synovial joint of ball and socket variety. The articular surface consists of glenoid fossa of scapula and head of humerus. It is a weak joint because the glenoid cavity is too small and shallow to hold the head of the humerus which is approximately four times the size of it. But its stability is maintained by coracoacromial arch, musculotendinious cuff and glenoid labrum. It is covered by joint capsule which is loose and it permits free movements except in the inferior portion where it is deficient. It consists of multiple ligaments which include glenohumeral, coracoacromial, coracohumeral and transverse humeral ligament. It consists of the following bursae (Fig. 22.1).

- Subacromial: Beneath the acromioclavicular joint
- Subscapularis: Beneath the subscapularis-muscle
- Subdeltoid: Beneath the deltoid muscle

Classification

The causes for shoulder pain can be classified as follows:

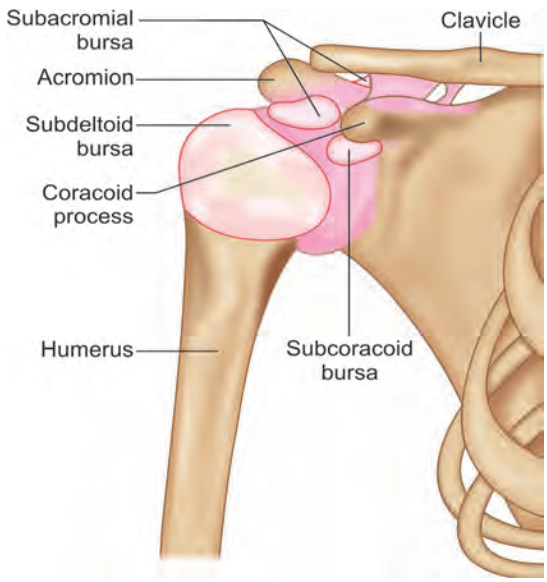


Fig. 22.1: Bursa around shoulder joint

Table 22.1: Muscles along with the nerve supply and mode of action (Fig. 22.2)

Muscle	*Origin*	*Insertion*	*Nerve supply*	*Action*
Supraspinatus	Medial 2/3rd of supraspinous fossa of scapula	Upper impression of greater tubercle of humerus	Suprascapular nerve	Abduction of arm up to 15°
Infraspinatus	Medial 2/3rd of infraspinous fossa of scapula	Middle impression of greater tubercle of humerus	Suprascapular nerve	Lateral rotation
Subscapularis	Medial 2/3rd of the subscapular fossa	Lesser tubercle of humerus	Upper and lower subscapular nerves	Adductor Medial rotation
Biceps	Short head arises from tip of corocoid process Long head arises from supraglenoid tubercle and labrum	Radial tuberosity	Musculocutaneous nerve	Flexor of elbow and arm Supinator of flexed forearm
Deltoid	Anterior border of the lateral 1/3rd of clavicle Lateral border of acromion Lower lip of the crest of spine of scapula	Deltoid tuberosity	Axillary nerve	Abduction Flexion Extension Medial and lateral rotation
Teres major	Lower 1/3rd of the dorsal surface of the lateral border and inferior angle of scapula	Medial lip of bicipital groove of the humerus	Lower scapular nerve	Adductor Medial rotation
Teres minor	Upper 2/3rd of the dorsal surface of the lateral border of scapula	Lowest impression of greater tubercle of humerus	Axillary nerve	Lateral rotation
Triceps	Long head—infraglenoid tubercle Lateral head—posterior side of humerus Medial head—posterior surface of humerus in termuscular septa	Posterior part of superior surface of olecranon process of ulna	Radial nerve	Extensor of elbow Supports head of humerus in abducted position of the arm

Non-traumatic

Intrinsic Causes

1. Glenohumeral

i. Rotator cuff tendinopathy
ii. Rotator cuff tear
iii. Subacromian bursitis
iv. Glenohumeral arthritis
v. Glenohumeral instability
vi. Labral tear

2. Extra glenohumeral

i. Bicipital tendinopathy
ii. Acromioclavicular arthritis
iii. Subscapular bursitis
iv. Distal clavicle osteolysis

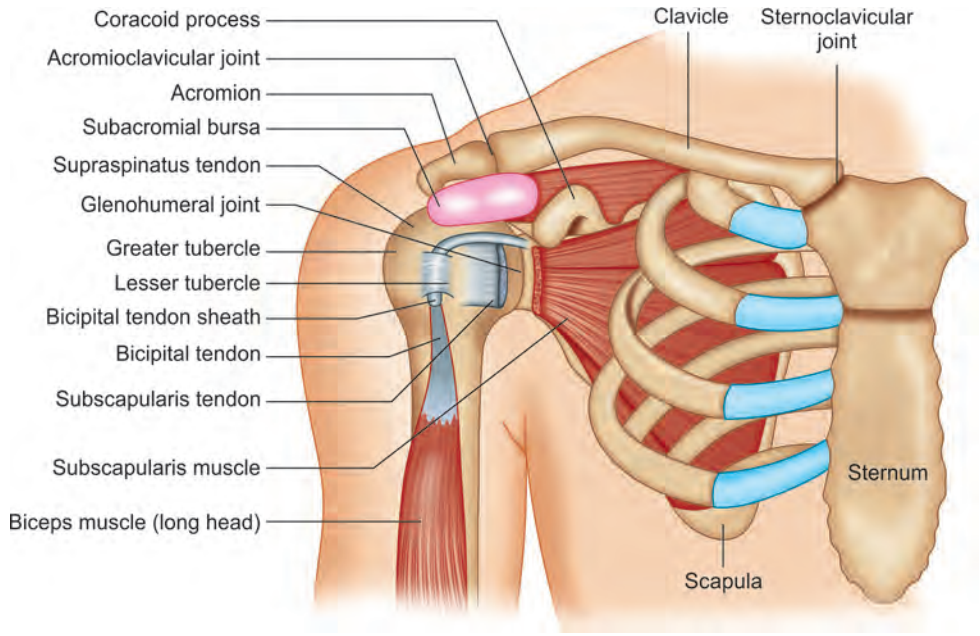


Fig. 22.2: Muscles around shoulder joint

Extrinsic Causes

1. Disc herniation with neural impingement at C5 or C6 level
2. Cervical spinal canal stenosis
3. Long thoracic and suprascapular neuralgia
4. Post-herpetic neuralgia involving C4, 5 nerve root
5. CRPS involving upper arm and shoulder
6. Referred pain
   - Myofascial pain syndrome (commonly trapezius)
   - Diaphragm irritation
   - Myocardial ischemia
   - Intrathoracic tumors

Traumatic

1. Fracture clavicle
2. Fracture humerus
3. Glenohumeral dislocation
4. Acromioclavicular ligament sprain

Red Flags[1]

These conditions should be identified as early as possible and should be referred to speciality centres for further management.

- Tumor
- Acute rotator cuff tear
- Unreduced dislocation
- Infection
- Unexplained significant sensory and motor deficit
- Pulmonary and vascular compromise

History Taking

Pain history should focus on onset, nature, duration, exacerbating and relieving factors, location, radiation and night pain. History also should focus on other areas of pain including neck and thoracic region. Significant comorbid conditions and systemic illness and their treatment history should be noted. Functional restriction in range of motion can be elicited from history itself which can help us in planning rehabilitation.

Physical Examination

Inspection

Inspection of shoulder should be done for the normal as well as the disease shoulder from front, side and back. Look for muscle wasting

and atrophy abnormal swelling, deformity (dislocations), scars, ecchymosis and venous distension. Look at neck and axillae for lymphadenopathy.

Palpation

Palpation includes glenohumeral joint, acromioclavicular and sternoclavicular joints, cervical spine, rotator cuff and bicipital groove. The coracoid process, acromion and scapula should also be palpated for any tenderness and deformity.

Range of Motion

Range of motion should be assessed for forward flexion, isolated abduction, horizontal adduction, external and internal rotation with arm at 0°, and external and internal rotation with the arm in abduction.

During abduction of the shoulder, the G-H joint is reported to contribute up to 120 degrees of the total arc of motion, with the remaining 60 degrees occurring at the scapulothoracic joint. Arm elevation beyond 90 degrees requires motion in other, more distal joints such as the A-C and S-C joint.

Apley's scratch test can be used to test range of motion. The patient attempts to touch the opposite scapula in two directions (Figs 22.3 and 22.4).

Fig. 22.3: Testing abduction and external rotation

Fig. 22.4: Testing adduction and internal rotation

The thumb tip of normal subjects will reach the T5–T10 level.

Muscle Strength

The following tests are done to check the rotator cuff muscle strength.

Empty Can Test[2]

- **Background:** To test the strength of supraspinatus muscle.
- **Posture:** Sitting or standing, shoulders in 90° abduction, 30° of horizontal adduction and full internal rotation.
- **Fixation:** The examiner places his hands on the upper side of the limb and exerts downward resistance (Fig. 22.5).

Fig. 22.5: Empty can test

- **Test:** The patient maintains this position against downwards resistance.
- **Pay attention:** Focus primarily for muscle-weakness and pain.

Belly Press Test

- **Background:** The belly press test may be valuable as specific test to rule out sub-scapular tears.
- **Posture:** Patient in sitting posture with hand of the affected arm placed on the abdomen (Fig. 22.6).
- **Fixation:** No fixation is applied.
- **Test:** Patient exerts pressure on the abdomen with the hand until maximal internal rotation.
- **Pay attention:** The patient feels weakness and cannot maintain maximal internal rotation. The elbow drops backwards, and internal rotation is lost. Pressure is exerted by extension of shoulder and flexion of the wrist.

Fig. 22.6: Belly press test

Infraspinatus and Teres Minor Strength

- **Background:** To test infraspinatus and teres minor strength.
- **Posture:** Patient arms by the side with elbows flexed at 90° (Fig. 22.7).
- **Fixation:** Examiner keeps his hands on side of the arm.
- **Test:** Patient is asked to externally rotate the arm against the examiners hand resistance.
- **Pay attention:** The patient's external rotation strength is compared to normal arm.

There are various other specific tests which will be discussed in later part of this chapter.

VARIOUS PATHOLOGICAL CONDITIONS AFFECTING SHOULDER

1. Degenerative Arthritis [OA] of Shoulder

Symptoms and Signs

- Localized constant aching pain around the shoulder and upper arm which gets worst with activity and relieved by rest and heat.
- Grating or popping sensation.
- Crepitus +/–
- Gradual decrease in functional ability
- Decreasing range of active and passive motions

Fig. 22.7: Infraspinatus and teres minor strength test

- Continued disuse results in muscle wasting and frozen shoulder.
- Primary OA is seen very rarely in clinical practice.

Investigation

Plain radiographs will show reduced joint space, osteophytes, subchondral sclerosis, cysts, and eburnation or advanced articular cartilage loss (Fig. 22.8).

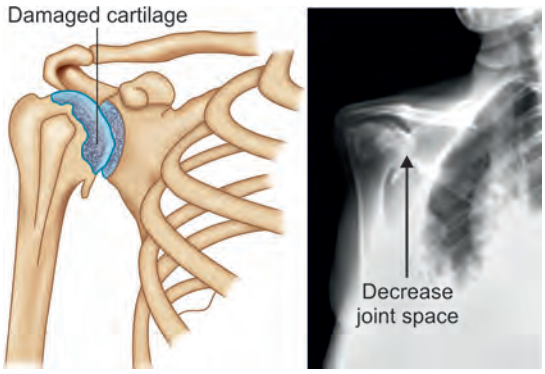


Fig. 22.8: X-ray of OA shoulder

Treatment

- Nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors
- Physical therapy.
- Local application of heat and cold modalities.
- Nonresponders: Intra-articular injection of local anesthetic and steroid under aseptic condition.

2. Disorders of Rotator Cuff

- Rotator cuff tendinopathy (Fig. 22.9).

Symptoms and Signs

- Anterior shoulder pain, insidious in onset and progressive in nature
- Radiating to the anterolateral aspect of the shoulder to the deltoid insertion.
- Tenderness is elicited in the subacromial region
- **Hawkins–Kennedy test:**[3] Passive internal rotation—painful (Fig. 22.10)
- **Neer's test:**[4] Passive forward elevation of arm—painful (Fig. 22.11)

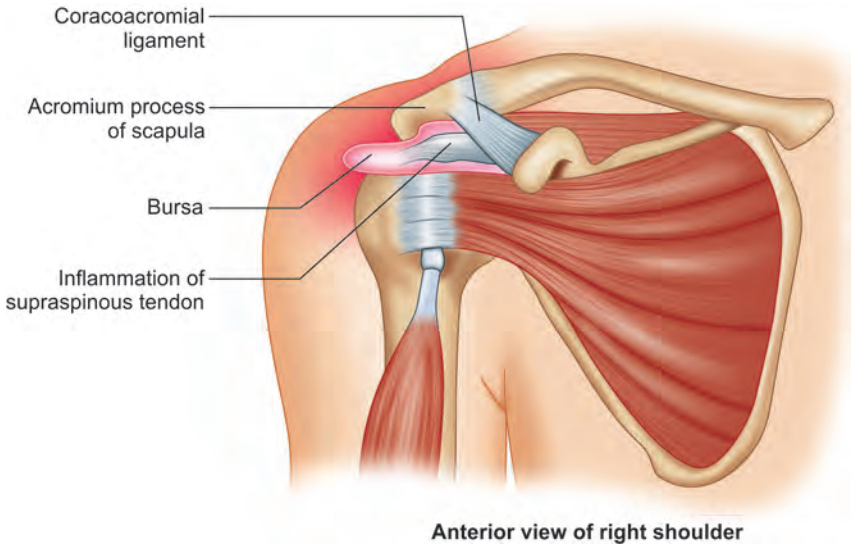


Fig. 22.9: Rotator cuff tendinopathy

Fig. 22.10: Hawkins Kennedy test

Fig. 22.11: Neer's test

Rotator Cuff Tear (Fig. 22.12)

Symptoms and signs

- Constant severe pain and night pain
- In partial tear, patient will have inability to elevate the above the level of shoulder without using the other arm to lift it.
- In complete tear, patient will have complete inability to reach above the shoulder and will have anterior migration of humeral head.
- In case of infraspinatus tear, patient will have difficulty in external rotation.
- Range of motion will be diminished more in active than in passive movement.
- **Drop arm test:**[5] Abduction of arm horizontally in the plane of scapula passively

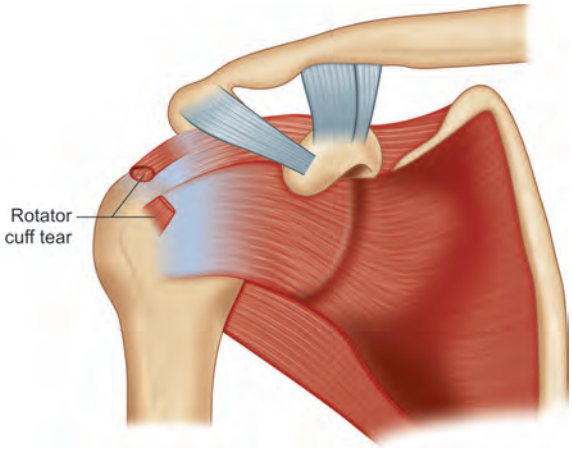


Fig. 22.12: Rotator cuff tear

Fig. 22.13a and b: Drop arm test

and while lowering the arm leaning towards the affected side will cause drop of arm in case of complete tear (Fig. 22.13a and b).

Investigation

USG and MRI can be done. USG is more cost-effective method than MRI in identifying rotator cuff tear.

Treatment

- Rest and avoidance of pain aggravating activities
- Pain modification techniques such as cryotherapy, infrared therapy, ultrasound, transcutaneous electric nerve stimulation, and acupuncture can provide symptomatic relief.
- USG-guided subacromial LA and steroid injection with no rotator cuff tear.
- Rehabilitation which includes gentle stretching programs and restoration of range of motion and muscle strengthening activities.
- Modification of working environment.
- Surgical intervention in case of patients not responding to conservative therapy after 3- to 6-month period

3. Acromioclavicular (AC) Joint Pain

Symptoms and Signs

- Pain when reaching across the chest.
- Unable to sleep on the affected shoulder
- Grinding sensation in the joint on first awakening.
- Tenderness over AC joint
- Downward traction or passive adduction increases pain.

Investigation

Plain radiographs, USG and MRI (when associated ligament injury is suspected).

Treatment

- Physical therapy.
- Local application of heat and cold also may be beneficial.
- USG-guided intra-articular injection of local anesthetic and steroid can be tried in case of failed conservative treatment.

4. Subdeltoid Bursitis

Symptoms and Signs

- Localized pain in the subdeltoid area, with referred pain often noted at the insertion of the deltoid at the deltoid tuberosity on the upper third of the humerus
- Unable to sleep on the affected shoulder
- Sharp, catching sensation when abducting the shoulder, especially on first awakening.
- Point tenderness over the acromion
- Passive elevation and medial rotation of the affected shoulder reproduce the pain, as do resisted abduction and lateral rotation.

Investigation

USG and MRI

Treatment

- Physical therapy.
- Local application of heat and cold
- USG-guided intra-articular injection of local anesthetic and steroid in case of failed conservative treatment.

5. Biceps Tendinitis (Fig. 22.14)

Symptoms and Signs

- Pain in the anterior shoulder that may radiate to the biceps muscle and it worsen with overhead activities.
- Nocturnal pain.
- Point tenderness in the bicipital groove.
- Speed test
  Patient holds the elbow in extension with the forearm supinated and then flexes the shoulder against resistance, thus reproducing the patient's pain (Fig. 22.15).
- Yergason test: Patient supinates the forearm against resistance with the forearm flexed. A positive test result occurs when pain refers to the bicipital groove (Fig. 22.16).

Investigation

USG and MRI

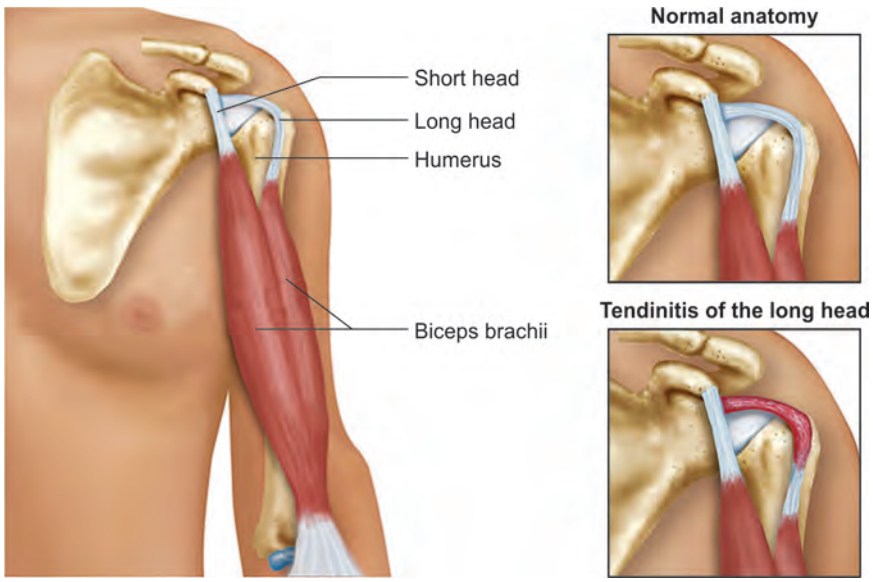


Fig. 22.14: Figure showing normal biceps tendon and inflamed long head of biceps which is more localised in bicipital groove

Fig. 22.15: Speed test

Fig. 22.16: Yergason test

Treatment

- Rest
- Local application of ice
- Anti-inflammatory medications.
- Physical therapy
- USG-guided local anesthetic and steroid injection in case of failed conservative method.
- Surgical intervention for patients with significant instability or with recalcitrant symptoms

6. Scapulocostal Syndrome

Symptoms and Signs

- Pain localized to the medial superior border of the scapula radiating into the neck, root of the shoulder, around the chest wall or down the arm, usually in an ulnar nerve distribution.
- Characteristic of pain: Aching, burning, or gnawing, and rarely as sharp or radicular.
- Sensory features+/-

- Weakness of the arm, without atrophy or neurophysiologic evidence of denervation
- Trigger point at the medial scapular border in a line extending from the scapular spine, after adducting the arm
- Extension and internal rotation of the arm also elicit the pain

Treatment

- Activity modification
- Physical therapy
- Anti-inflammatory medications
- Injection of LA with steroid into the region of the medial superior scapular border can confirm diagnosis and also have therapeutic value.

7. C7 Radiculopathy

Symptoms and Signs

- Sharp pain usually descends the posterior aspect of the upper arm into the middle finger.
- Weakness of the triceps and wrist extensors.
- Diminution of the triceps reflex.
- Hypesthesia in the C7 dermatome.
- Spurlings test positive

Investigation

MRI cervical spine and nerve conduction study.

Treatment

- Conservative with anti-neuropathic drugs like gabapentin and amitriptyline.
- Physical therapy
- Cervical epidural steroid injection in case of failed conservative method
- When associated with significant motor weakness, then surgical decompression is preferred.

8. Suprascapular Nerve Entrapment

Symptoms and Signs

- Deep, poorly circumscribed pain over posterior and lateral aspects of the shoulder.
- Long standing cases, it leads to atrophy of the supraspinatus and infraspinatus muscles which are confirmed by difficulty in initiating abduction and rotation at the glenohumeral joint.
- Tenderness in suprascapular notch.
- Cross-body adduction test: Adducting the extended arm passively—across the midline is extremely painful
- Suprascapular nerve block can be done with local anesthetic and steroid for failed conservative method.

REFERENCES

1. Tarun Kumar Reddy Rammurthy Kulkarni. Evaluation of shoulder joint. In: Das G, editor. Clinical methods in pain medicine. New Delhi: CBS Publishers and Distributors; 2014.p.50–62.
2. Jobe FW, Jobe CM. Painful athletic injuries of the shoulder. Clin Orthop Relat Res 1983;173:117–24.
3. Hawkins RJ, Kennedy JC. Impingement syndrome in athletes. Am J Sports Med. 1980;8:151–8.
4. Neer CS 2nd. Impingement lesions. ClinOrthop Relat Res.1983;183:70–7.
5. Maarten Hendrik Moen, et al. Clinical tests in shoulder examination: How to perform them?.Br J Sports Medicine. 2010;44:370–5.

CHAPTER

23

Knee Pain

R Gurumoorthi

FUNCTIONAL ANATOMY

The knee joint is the largest and complex joint because of the fusion of three joints, i.e medial and lateral femorotibial and femoropatellar joint.[1]

- *Type*: Synovial hinge joint.
- *Articular surface*: The femoral condyles articulate with the tibia condyles below and behind and with the patella in front.
- Fibrous capsule: Thin and deficient anteriorly, reinforced by multiple ligaments and lined by synovial membrane.
- *Ligaments*: Intra-articular and extra-articular ligaments.
  - Patellar ligament: Extends from posterior surface of apex of patella to the upper part of tibial tuberosity.
  - Tibial (medial) collateral ligament: Extends from medial epicondyle of femur to tibial medial condyle.
  - Fibular (lateral) collateral ligament: Extends from lateral epicondyle of femur to head of the fibula.
  - Anterior cruciate ligament (ACL): Extends from anterior part of intercondylar area of tibia to the posteriomedial surface of lateral condyle of femur.
  - Posterior cruciate ligament (PCL): Extends from posterior part of intercondylar area of tibia to the anteriolateral surface of medial condyle of femur.
- Medial meniscus and lateral meniscus are fibrocartilaginous disc, medial being semicircular, whereas lateral is circular. They deepen the articular surfaces of the condyles.

Anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) maintain the anterioposterior stability. The menisci located medially and laterally function as shock absorbers, lubricate joint movements and also send proprioceptive impulses (Fig. 23.1).

Bursae around Knee Joint

13 bursae have been described around the knee joint—four being anterior, four being-lateral and five being medial. A few important includes

- Prepatellar bursa
- Infrapatellar bursa
- Suprapatellar bursa
- Pes anserinus

Nerve Supply

- Femoral, Sciatic and Obturator nerves

Red Flags[2]

1. An acutely effused knee with history of trauma: Fracture must be ruled out
2. A red, hot knee joint, consideration must be given to septic arthritis.
3. Patients with systemic symptoms or multi-joint involvement. These patients are likely to have a systemic condition and should be appropriately evaluated.

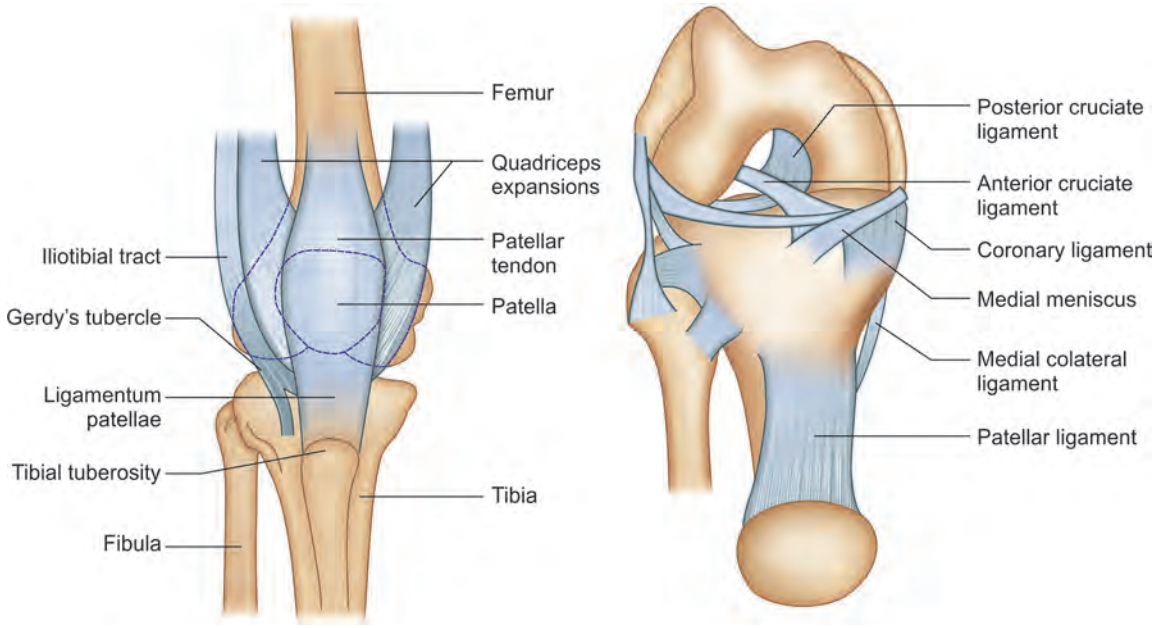


Fig. 23.1: Ligaments in and around the knee joint

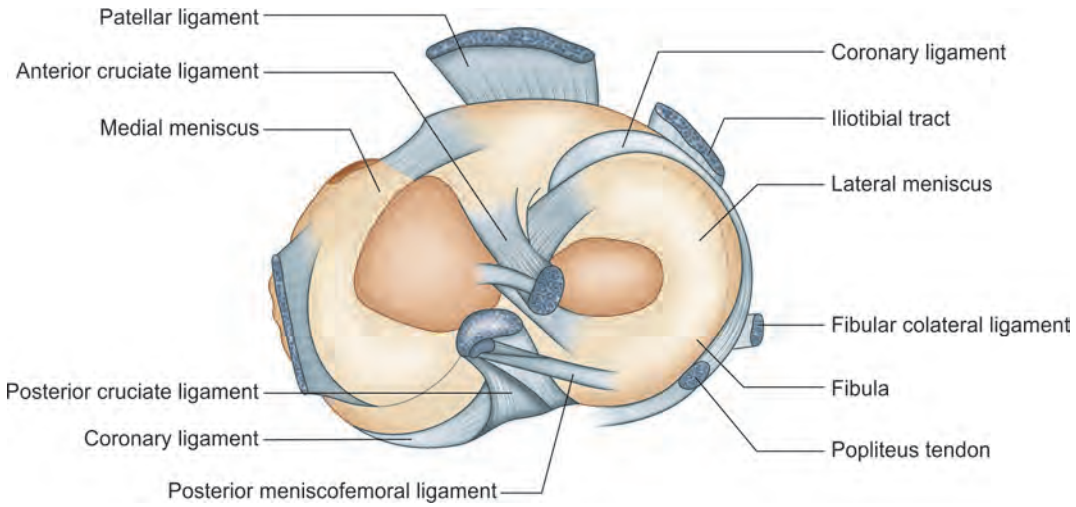


Fig. 23.2: Ligaments and cartilages in and around knee

General Approach to the Patient with Knee Pain and Clues from the History

A thorough history plays a very important role in determining the etiology of knee pathology.

- Main symptoms
  - Pain
  - Swelling
- Mechanical
  - Gelling
  - Locking
  - Pseudolocking
  - Popping
  - Buckling
  - Crepitation

Pain[2]

It may be of two reasons. Either it may be due to pathology in knee or referred from other areas. Detailed history and examination will help in differentiating it.
Look for following characteristic in pain

- Onset (rapid or insidious)
- Location (anterior, medial, lateral or posterior of knee)
- Duration (acute or chronic)
- Severity (mild, moderate, severe)
- Quality (e.g. dull, sharp, aching)
- Aggravating and alleviating factors

Referred Pain

- Facet joint
- Lumbar disc
- L3/L4 nerve root pain
- Hip pathologies
- Myofascial pain.

Effusion

Rapid onset of an effusion may be due to hemoarthrosis, fracture, dislocation, meniscal tear and ligamentous tear. Slower onset effusion may be due to meniscal injury or ligament sprain. Recurrent effusion is suggestive of meniscal injury.

Mechanical Symptom

Gelling	Degenerative joint disease
Locking	Meniscal tear
Pseudo locking	Crystal, plica, loose body
Popping	Ligamentous injury

Mechanism of Injury

A direct blow to the anterior of knee or quick accelerating injury of knee, e.g. dashboard of a car when hitting the break suddenly can injure PCL. Quick decelerating injury like quick stops or sudden sharp turn can injure ACL. A valgus force on the knee can injure the medial collateral ligament and vis-à-vis varus force can cause injury to lateral collateral ligament. Sudden twisting movement of knee with foot planted can injure meniscus.

The overall health of the patient should be assessed, including lifestyle, sports activity, any medical conditions, medication usage and malignancy.

Examination

Evaluation of knee requires complete exposure of the involved knee as well as the other knee for comparison.

- Inspection
- Palpation
- Range of motion
- Special maneuvers

Inspection	Range of motion
1. Gait 2. Allignment 3. Atrophy 4. Swelling 5. Deformity	1. Passive and active • Flexion (normal 130–150°) • Flexion (normal 0–10°) 2. Patellar tracking
Palpation	**Specific maneuvers**
1. Tibial tuberosity of patella 2. Bursae 3. Joint lines 4. Popliteal fossa 5. Intra- and extra-articular swelling • Ballotment • Milking	1. Valgus and varus strees test 2. Anterior and posterior drawer tests 3. Lachman test 4. Tibial sag test 5. Apley's compression test 6. McMurray's test

Investigation

CBC, ESR, CRP to rule out red flags. In X-ray knee standing AP and lateral view is done to rule out red flags and also in grading OA. In case of inflammatory arthropathy, uric acid, RA, Anti-CCP, ANA, etc can be done. Effusion fluid can be analysed for infective and inflammatory arthropathy.

COMMON CLINICAL PRESENTATIONS

Suprapatellar Bursitis

Signs and Symptoms

- Anterior knee pain above the patella radiating superiorly into the distal anterior thigh.

- Unable to kneel or walk downstairs
- Sharp, catching sensation with movement of the knee, especially on first awakening.
- Swelling above and around patella.
- Tenderness in anterior knee just above the patella.
- Palpation: Boggy feeling
- Movements: Passive flexion and active resisted extension of the knee reproduce the pain.
- Systemic symptoms including fever and malaise and local signs.

Treatment

- Rest
- Hot and cold fomentation
- NSAIDs and COX-2 inhibitors
- USG guided LA and steroid
- Physical therapy

Prepatellar Bursitis

It is also known as housemaid's knee because of its common prevalence in people whose job requires prolonged crawling on knee.

Signs and Symptoms

- Pain in the anterior knee over the patella radiating superiorly and inferiorly into the area surrounding the knee.
- Inability in kneeling or walking down-stairs.
- Sharp, catching sensation with movement of knee on first awakening

Treatment

- Rest
- Hot and cold fermentation
- NSAIDs and COX-2 inhibitors
- USG guided LA and steroid
- Physical therapy

PES ANSERINE BURSITIS

Signs and Symptoms

- Localised, constant and aching pain over the medial knee joint.
- Aggravated by activity, especially walking downstairs
- Relieved by rest and hot fomentation.
- Sleep disturbance +
- Point tenderness in the anterior knee just below the medial knee joint at the tendinous insertion of the pes anserine.
- Swelling surrounding the bursa is often present.
- Active resisted flexion of the knee reproduces the pain.

DEEP INFRAPATELLAR BURSITIS

Signs and Symptoms

- Pain in the anterior knee below the patella radiating inferiorly into the area surrounding the knee.
- Unable to kneel or walk downstairs.
- Sharp, catching sensation with range of motion of the knee, especially on first arising
- Point tenderness in the anterior knee just below the patella.
- Swelling surrounding the lower patella
- Passive flexion and active resisted extension of the knee reproduce the pain.

QUADRICEPS EXPANSION SYNDROME

- Pain at the superior pole of the patella.
- Patient notes increased pain on walking down slopes or downstairs
- Activity of the knee makes the pain worse
- Rest and heat provide some relief.
- The pain is constant, is characterized as aching, and may interfere with sleep.
- Tenderness under the superior edge of the patella that occurs more commonly on the medial side.
- Patients exhibit a positive knee extension test on active resisted extension of the knee that reproduces the pain.
- Treatment protocol same as above.

PATELLOFEMORAL SYNDROME (PFS)

It is because of repetitive microtrauma, overuse and underlying anatomic anomalies which allow for abnormal tracking of the patella. Adolescents and young adults are most commonly affected, and females slightly more than males.

Signs and Symptoms

- Prior retropatellar dull or achy pain aggravated with any activities that stress the patella like ascending or descending stairs, squats or knee bends and sometimes complain of pain after prolonged sitting with flexed knees ("Theatre sign").
- Tenderness on the medial and lateral facets on the underside of the patella.
- Compression of the patella on the femoral condyle pain, as may grasping the patella firmly on both sides and asking the patient to activate the quad muscle.
- PFS is a clinical diagnosis, and radiographs are usually not indicated.

Treatment

- In the acute phase, NSAIDs can be helpful.
- Ice massage or packs for 20–30 min per session several times a day can help control of pain and inflammation.
- As the acute phase resolves, physical therapy in a structured program and/or through home exercises. Surgical correction of the underlying anatomic problems, such as weak quadriceps muscles and retinacular stretching can prevent the improper tracking.

LIGAMENT TEARS (ACL)

It occurs due to hyperextension or contact injury such as direct valgus force to the leg when the foot is planted.

Signs and Symptoms

- Hears or feels a "pop,"experiences a great deal of pain, and unable to continue the activity.
- Associated hemoarthrosis in complete tear.
- Lachman test and anterior drawer test will be positive

Treatment

- Rest, crutches, ice, pain control, and physical therapy.
- Surgical correction in case of complete tear.

The PCL will be rarely injured unless the knee trauma is severe as in case of car dashboard injury and it is the last to be affected in the kinetic chain under most circumstances.

THE MEDIAL AND LATERAL COLLATERAL LIGAMENTS (MCL AND LCL)

- These can also be injured with varus or valgus forces.
- Pain and tenderness over corresponding site
- MCL and LCL testing is done with the knee in full extension and 20° of flexion, with varus and valgus stress being applied to the knee in both positions. The examiner, while examining, feels for an "opening" or side to side movement of the joint space.

Treatment

- Rest, ice, pain killers and physical therapy.
- Orthopedic referral, but usually does not require surgery.

MENISCAL TEARS

It occurs with knee partially flexed when a twisting valgus or varus injury occurs. The medial meniscus is more commonly injured than the lateral.

Signs and Symptoms

- Locking, catching and popping
- Tenderness over the joint line
- McMurray test—positive test may help in diagnosing, but a negative test does not rule out a meniscal tear

Treatment

- Rest, analgesics, possible orthopaedic referral for surgical correction once acute phase settles.

PATELLAR DISLOCATION

It is caused by direct trauma or by an indirect mechanism with the foot planted and twisting the torso quickly as in swinging at a baseball. Dislocation almost always laterally. It usually relocates spontaneously, but sometimes a manual reduction is required

Signs and Symptoms

The patellar apprehension test is used to evaluate patellar instability.

Treatment

Pain control and close follow up.

OSTEOARTHRITIS

In older patients, particularly those over 50 years of age, osteoarthritis (OA) of the knee joint is extremely common. These patients typically complain of diffuse knee pain that worsens with weight bearing activities, and they often report some morning stiffness. In general, the pain is chronic but can be exacerbated by heavy activity causing acute flare ups, and patients may even report episodes of swelling.

On physical examination, there may occasionally be a visible/palpable effusion, but stability of the knee (as described earlier) will be intact on testing. Tenderness over joint line will be more pronounced over medial joint line. Range of movements can be restricted with end bony resistance in passive flexion. Crepitus is a common finding, but does not necessarily relate to the degree of OA. OA can be associated with meniscal tear and can have corresponding test positive.

X-ray knee standing AP and lateral view is considered to grade OA knee. MRI can help in localised exact compartment and associated meniscal and ligament injury. Kellgren and Lawrence classification[3] of OA knee is commonly used (Table 23.1).

Table 23.1: Kellgren and Lawrence classification of OA knee

Grade	*Description*
0	No radiographic features of osteoarthritis
1	Possible joint space narrowing and osteophyte formation
2	Definite osteophyte formation with possible joint space narrowing
3	Multiple osteophytes, definite joint space narrowing, sclerosis and possible bony deformity
4	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity

Treatment

- Analgesics, topical application, heat therapy and physical rehabilitation.
- Intervention including steroid (not advisable), platelet rich plasma, prolotherapy and viscous supplementation
- For Grade 3 and above, it is better to proceed for knee replacement and for those who are not willing can undergo genicular nerve block as palliative procedure.

REFERENCES

1. Elaine A, Jill K, Emily G. A practical approach to orthopaedic medicine. Edinburg: Churchill Livingstone Elsevier;2010.
2. Sourav I, Aniketa B, Saikat M. Evaluation of knee pain. In: Das G. editor. Clinical methods in pain medicine. New Delhi: CBS Publishers & Distributors; 2014. P. 151–63.
3. Kellgren JH. Lawrence JS. Radiological assessment of osteo-arthrosis. Annals of the rheumatic disease. 1957;16 (4): 494–502.

CHAPTER

24

Nonpharmacological Management of Joint Pain

Pampa De

REHABILITATION PRINCIPLES OF SHOULDER PAIN

The acronym RICE which stands for rest, ice, compression and elevation is frequently used in acute phase of rehabilitation. Rest should be relative for the affected part. It is important to maintain cardiovascular fitness, strength and flexibility during this phase. During the acute phase cryotherapy can be used to decrease pain, inflammation, muscle guarding, edema and local blood flow.[1] Heat increases blood flow, reduces muscle spasm and thereby pain and can be utilized in acute phase of rehabilitation for chronic injuries.[2] High frequency electrical stimulation in acute phase can be used to decrease muscle guarding and increase local circulation.[3] The recovery phase of rehabilitation is achieved when the pain is adequately controlled, tissue healing has occurred as indicated by full pain free range of motion and ability to participate in strengthening exercises.[4] Strength and flexibility imbalances, maladaptive movement patterns and muscle substitution should be corrected in this phase of rehabilitation. Open kinetic chain exercises are used to correct the strength deficits and closed kinetic chain exercises are used to provide joint stabilization through muscular contraction.Towards the end of the recovery phase patient can begin the functional stage of rehabilitation when the injured limb has regained 75 to 80% of normal strength as compared to the non-injured limb.

Rehabilitation Principle of Knee Pain

For the lower limb especially the term kinetic chain assessment is important in the process of rehabilitation. Kinetic chain refers to the model of human motion that analyses and treats dysfunction along connected anatomic regions, rather than focussing only on the location of pain. Biomechanical deficits that refer to any deficiency in range of motion, flexibility, strength, endurance or motor control are to be addressed. Muscle imbalance in agonists and antagonists need to be corrected. Functional exercises which refer to exercise movements that stimulate muscle groups to work in a way they normally work during functional and athletic activities. For the ligament injuries in the knee, the usual conservative methods of ice application, elevation, compression, application of a knee immobilizer or hinged knee brace, crutch ambulation, gentle knee flexion and extension exercises, quadriceps exercises, straight leg raises, walking, cycling, functional knee brace during moderate activities are applied. Young healthy athletes or cases with grade three MCL tear may require surgery and in them meniscal tears may require arthroscopic repair.

Rehabilitation Principle in Osteoarthritis

Exercise: Land-based therapeutic exercise has been shown to reduce pain and improve physical function for people with OA of the knee. Both high intensity and low intensity

aerobic exercise improve functional status, gait, pain and aerobic capacity.[5]

Physical modalities: Ice massage improves range of motion, function and knee strength. Cold packs decrease swelling. Short wave diathermy may provide significant improvements for knee OA. TENS and acupuncture like TENS might be effective in pain control. Results of laser therapy are conflicting, depends upon the method of application.[6]

Manual and mechanical therapies: No evidence is available for manual therapies in OA. For pain there is evidence that real acupuncture is more effective than sham acupuncture.

Upper limb orthoses and manipulation aids: A little evidence specific for OA.

Lower limb orthoses and mobility aids: Limited evidence is available that a knee brace is beneficial for OA of the medial compartment of knee when compared to medical treatment alone or neoprene sleeve. There is limited evidence that a laterally wedged insole decreases NSAID intake compared with neutral insole.

Rehabilitation Principle in Rheumatoid Arthritis

Rest: Systemic bed rest needed varies with the individual from complete bedrest to a short nap during the day. Localized rest to individual joints may include wearing a splint to support the joint during activity or lying in non-weight bearing position.

Exercise: Dynamic exercise therapy is effective at increasing aerobic capacity and muscle strength. There is strong evidence for the efficacy of instruction on joint protection. Tai chi does not seem to exacerbate symptoms of rheumatoid arthritis and has significant benefits on lower extremity range of motion.

Physical modalities: Hot and ice pack applications, cryotherapy and faradic baths on joint swelling are effective. Hand ultrasound increases grip strength and reduce the number of swollen and painful joints. Balneotherapy is helpful in RA. Electrical stimulation has a beneficial effect on grip strength and fatigue resistance for RA patients with muscle atrophy of the hand. Acupuncture like TENS seems beneficial for reducing pain intensity and improving muscle power while conversely conventional TENS shows no benefit. Low level laser therapy could be considered for short term relief of pain and morning stiffness for RA patients because it has a few side effects.

Manual and mechanical therapies: Electroacupuncture may be beneficial to reduce knee pain in patients with RA.

Upper limb orthoses and manipulation aids: There is insufficient evidence about the effect of working wrist splint in pain or function in people with RA, some rather decreses the grip strength and dexterity. But there is evidence that patients prefer to wear them.

Lower limb orthoses and mobility aids: Extra depth shoes and molded insoles decrease pain during weight bearing activities like standing, walking and stair climbing. Insoles may be effective in preventing progression of hallux adductus angle.

REFERENCES

1. Herring S. Rehabilitation of muscle injuries. Med Sci Sports Exerc. 1990;22: 453.
2. Kaul M, Herring SA. Superficial heat and cold. Phys Sports Med. 1994;22:65.
3. Windsor R, Lester JP, Herring SA. Electrical stimulation in clinical practice. Phys sports Med.1993;21:85.
4. KIbler W.A framework for sports medicine. Phys Med Rehabil Clin North Am. 1994; 5:1.
5. Flynn JM, Kocher MS, Ganley TJ. Osteochondritis dessicans of the knee. J Pediatr Orthop. 2004; 22(4): 434–43.
6. Watterson JR, Esdaile JM. Therapeutic mechanisms and clinical potential in osteoarthritis of the knee. J Am Acad Orthop surg. 2000;8(5):277–84.

CHAPTER

25

Management of Joint Pain

Samarjit Dey and R Gurumoorthi

Joint pain is one of the common causes for morbidity and decreased quality of life. Joint pain is one of the areas where patient tries to treat it by self medication or alternate medicine claiming that analgesics, if taken for joint pain then have to take it for longer duration which can cause renal and gastric problems. Only a few of those patient seek medical advice for joint pain and surprisingly most of them are treated by analgesics, interventions or surgery without considering other factors involved in joint pain. Joint pain has to be treated in multidisciplinary method to sustain pain free joint.

Every patient should be ruled out of red flags[1,2] in each visit. It includes acutely effused joint with history of trauma where fracture must be ruled out. A red, hot joint, consideration must be given to septic arthritis. Patients with systemic symptoms or multijoint involvement are likely to have a systemic condition and should be appropriately evaluated. X-ray showing mass with cortical erosion should be referred immediately for further evaluation.

Joint pain should be considered in all four including physical, psychological, socioeconomic and spiritual. There are certain conditions like ankylosing spondylitis where physical rehabilitation is more important as these diseases are difficult to treat in established conditions. In physical treatment of pain, there are multiple options including rest, heat or cold therapy, analgesics, exercise therapy, intervention procedures including steroid, viscous, platelet rich plasma etc, intervention physiotherapy and finally surgery.

The word 'Rest' does not indicate bed rest. It is usually advised for 2–3 weeks as most of acute pain conditions weans off. In case of acute pain, cold therapy is advised and in case of chronic pain, heat therapy may be preferred. Cold therapy produces vasoconstriction, thereby edema and congestion can be reduced. Patient lifestyle should be evaluated and possible ergonomic corrections should be advised.

Analgesics form the backbone of joint pain management. WHO ladder had been advised for guiding analgesic usage. Mild form of joint pain can be managed with paracetamol up to 4 g/day. Due to its lower side effect profile it is always preferred. NSAIDs can be considered for acute onset pain where there is more involvement of inflammatory pathway like trauma, inflammation, etc. It had been advised to use for 5 days only along with gastric protecting agents like proton pump inhibitors.[3] Among NSAIDs, there are two groups of drug which includes non-specific inhibitors and specific COX-2 inhibitors. Non-specific inhibitors like diclofenac, mefenamic acid, etc. are effective in treating acute pain but it has added side effects because of blocking COX-1 which has protective role in gastric and renal system, thereby leading to gastritis and renal damage.[1]

COX-2 inhibitors like celecoxib, etoricoxib, etc. are specific for inflammatory pathway without renal and gastric damage. Though initially claimed to have this advantage, now some drugs had been withdrawn from market due to increased cardiac mortality.[4] All NSAIDs should be avoided in patient with cardiac, gastric, renal, asthma and bleeding disorders. For moderate pain, weak opioids like tramadol can be added keeping in mind about dependence. Strong opioids can be added for severe pain but it needs trained doctors who can take care of opioids side effect which can be life threatening including respiratory depression, drug abuse, etc.

In case of any joint pain lasting more than 3 months, neuropathic pain sets in along with nociceptive pain. In this case, antineuropathic drugs have to be added, which includes tricyclic antidepressants like amitriptyline 25 mg HS, SNRI like duloxetine 20 mg HS and anticonvulsants like gabapentine 300 mg HS and dose titrated according to response. Steroids can be used as last line analgesic and is effective in controlling nociceptive and neuropathic pain. It can be used orally, deep intramuscular depot injection and direct joint injection. There had been strong debate over further damage of joint cartilage with steroid usage. It had been recommended strongly in inflammatory arthropathy.

In case of inflammatory arthropathy, in addition to palliative analgesics, they should be started on disease modifying drugs which includes methotrexate, chloroquine, sulfasalazine, etc. Mild form of disease can be treated with sulfasalazine or chloroquine. Severe form of inflammatory arthropathy is treated with 15–25 mg methotrexate injection weekly along with folic acid and other oral DMARDs. In case of non-responsive patient to DMARDs, they should be referred to rheumatologist for immunomodulators.

In case of degenerative joint pain, interventions including prolotherapy with dextrose, ozone and viscous supplementation can be advised in early conditions. Platelet rich plasma can be advised in mild to moderate form of disease. Those patients with severe joint pain with bony deformity are advised for surgical correction. Psychological opinion can be sought in case of coexisting depression associated with pain. Once pain is controlled with above measures, patient is referred for physical and occupational rehabilitation.

REFERENCES

1. Judd DB, Kim DH. Foot fractures misdiagnosed as ankle sprains. Am Fam Physician. 2002;68:785–94.
2. Bourne RB, Rorabeck CH. Compartment syndromes of the lower leg. Clin Orthop. 1989;240:97–104.
3. Arroyo M, Lanas A. NSAIDs-induced gastrointestinal damage Review. Minerva Gastroenterol Dietol. 2006 Sep; 52(3):249–59.
4. Davies NM, Jamali F. COX-2 selective inhibitors cardiac toxicity: Getting to the heart of the matter. J Pharm Sci. 2004 Oct 29;7(3):332–6.

CHAPTER

26

Myths in Joint Pain

R Gurumoorthi

There are many misbelieves (myths) regarding joint pain not only among the general population but also among the treating physicians. Low level of education among the population is considered as an important factor for the prevalence of these myths. These myths are also difficult to remove or eradicate from the minds of the people or treating physicians. These myths are obstacles in the management of the joint pain. Understanding and accepting the facts help in the proper management of the joint pain.

1. Increasing age is the main factor in developing arthritis.

Fact: Degenerative osteoarthritis is very common in increasing age[1] and any arthritis occurring in younger age should be suspected for infective and inflammatory arthritis.[2]

With increasing age, due to wear and tear of joint, they are prone to develop degenerative arthritis. Even in those patients, pain is not always directly related to actual joint damage. It is highly variable with patient with clinical sign of osteoarthritis will not have any pain. In case of younger age group, inflammatory arthritis should be considered.

2. Joint which is swollen, warm and red is infective in etiology.

Fact: Same features can be seen in inflammatory arthropathy especially in gouty arthritis which can be monoarticular.

Gouty arthritis is due to deposition of monosodium urate [MSD] crystals in joint. It triggers inflammation which can lead to painful, swollen, warm and red joint. In early gout, only 1 or 2 joints are usually involved. The most common sites of gouty arthritis are the great toe, ankle, wrist, finger joints, and knee.[3] Gout attacks begin abruptly and typically reach maximum intensity within 8–12 hours. It is difficult to differentiate it from septic arthritis. In this case, joint fluid tap will help in differentiating both. Presence of negatively birefringence MSD crystals in polarized light with red filter will differentiate it from septic arthritis which has sensitivity of 84% and specificity of 100%.

3. Patient had been prescribed 20 mg methotrexate IM weekly, sulfasalazine 500 mg BD, prednisolone 10 mg OD for rheumatoid arthritis and patient came back to doctor stating that disease and pain is not getting down even after taking for 1 week.

Fact: Methotrexate is relatively rapid onset DMARDs but it takes nearly 6–8 weeks for its action to be seen clinically.

Drugs should not be stopped at least for these periods to assess need of further dose increment. Two-thirds of patients develop some clinical improvement as a result of therapy with any of these agents, although the induction of true remissions is unusual. In addition to clinical improvement, there is frequently an improvement in serologic evidence of disease activity, and titers of rheumatoid factor C-reactive protein and ESR frequently decline.[1]

4. Patient with shoulder pain with serum uric acid of 10 mg/dl should be treated for gouty arthritis.

Fact: Shoulder and spine are very rarely involved in gouty arthritis and just elevated serum uric acid without clinical features need not to be treated.

Measurement of serum uric acid is the most misused test in the diagnosis of gout. Approximately 25% of the population has a history of elevated serum uric acid, but only a minority of patients with hyperuricemia develops gout.[3] Thus, an abnormally high serum uric acid level does not indicate or predict gout. Asymptomatic hyperuricemia generally should not be treated. However, patients with levels higher than 11 mg/dL and overexcretion of uric acid are at increased risk for renal stones and renal impairment; therefore, renal function should be monitored in these individuals.

5. Topical application of NSAID is more safe and does not have any systemic side effects in arthritis.

Fact: Topical application of NSAID will also be absorbed systemically and can cause gastritis and renal damage.

It had been believed that when NSAID is applied topically will act only on that site and do not be absorbed systemically, thus no side effects. It had been proved that analgesic action due to topical NSAID is very minimal and mostly action is due to placebo effect. It will be absorbed systemically and will cause gastritis and renal damage, though less intense than oral or systemic NSAID. It can also cause local skin damage and reaction.[4]

6. HLA-B27 testing is mandatory for diagnosing Spondyloarthropathies.

Fact: Of the subtypes of SpA, AS is the most prevalent followed by undifferentiated SpA. The prevalence of HLA-B27 within patient populations with SpA ranges 50% to 95%. SpAs occur in about 2% of the general population and in just over 10% of HLA-B27 positive individuals. HLA-B27 testing is included in the ASAS classification criteria. The Amor criteria score allots a score of +2 to the presence of HLA-B27 amongst numerous other factors. However, given that SpA occurs in only approximately 10% of HLA-B27 individuals, the positive predictive value for disease is relatively low. Thus, HLA-B27 testing is generally not clinically useful by itself.

REFERENCES

1. David TF. Osteoarthritis. In: Anthony SF, editor. Harrison's rheumatology. New York: McGraw- Hill; 2010. P. 224–34.
2. Peter EL. Rheumatoid arthritis. In: Anthony SF, editor. Harrison's rheumatology. New York: McGraw-Hill; 2010. P. 82–99.
3. Akahoshi T, Murakami Y, Kitasato H. Recent advances in crystal-induced acute inflammation. Curr Opin Rheumatol. 2007 Mar; 19(2):146–50.
4. Derry S, Conaghan P, Da Silva JA, Wiffen PJ, Moore RA. Topical NSAIDs for chronic musculoskeletal pain in adults. Cochrane Database Syst Rev. 2016 Apr;4:CD007400.

SECTION

VI

Cancer Pain Management

Mayank Gupta (Section Editor)

27. Cancer Pain: What is Special?
28. Pharmacotherapy in Cancer Pain
29. Interventions in Cancer Pain
30. Palliative Care in Cancer
31. Myths in Cancer Pain

CHAPTER

27

Cancer Pain: What is Special?

Mayank Gupta

Pain is one of the most common and distressing symptoms in cancer. An estimated one-third (24–60%) and two-third (62–86%) of patients with cancer and advanced cancer respectively suffer from pain with more than one-third having moderate to severe pain.[1] ***Is am afraid not of cancer but pain!***—the phrase frequently heard by physicians working with cancer patients and very well reflects the true burden. Considering the magnitude of unrelieved pain and its adverse psycho-physical consequences; pain has been declared as the ***fifth vital sign*** by the Joint Committee on Accreditation of Health Organizations (1999).[2]

Etiology

Cancer pain is usually **multi-factorial** in origin and may be due to causes as given in Table 27.1.

Table 27.1: Cancer pain etiology and putative mechanisms

Etiology	*Mechanisms*
1. Due to tumor itself	**a. Compression** (of nerves/nerve plexuses/spinal cord/blood vessels causing ischemia, etc.). **b. Infiltration** (Nerves/Bones) **c. Stretching** (Liver capsule)
2. Iatrogenic	**a. Post-surgery** (phantom limb pain/stump pain/post-mastectomy pain/post-surgical chronic pain). **b. Chemotherapy** induced neuropathic pain **c. Radiotherapy** induced neuropathic pain
3. Debility	Bed sore, constipation, bladder spasm, etc.
4. Co-morbidities ***Learning point: All pains in cancer are not cancer pain***	Sciatica, back pain Arthritis Angina
5. Other causes	Psychological pain Spiritual pain Social pain

Total Pain

Cancer pain is not only multifactorial but also multidimensional in nature. Pain is said to exist in bi-directional cause–effect relationship with the physical, psychological, spiritual and social functioning of the patients and their families (Fig. 27.1). When considering all these contributing components of the pain experience, it is termed "***Total Pain***".

Classification of Cancer Pain

Cancer pain can be broadly classified into **nociceptive** (activation of the nociceptors) or **neuropathic** pain (damage to the nervous system itself) (Fig. 27.2). Cancer pain frequently results from mixed mechanisms and has been found to be somatic, visceral, neuropathic and mixed in 35%, 17%, 9% and

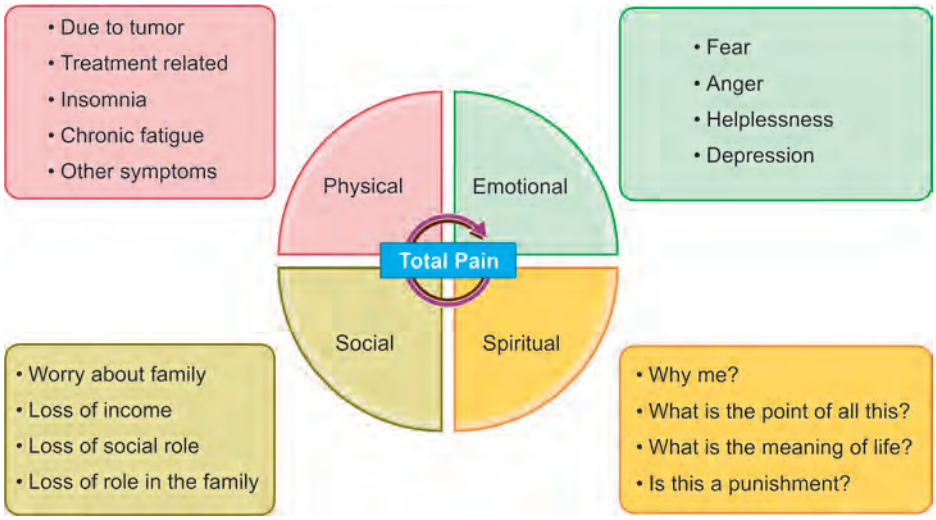


Fig. 27.1: Concept of total pain

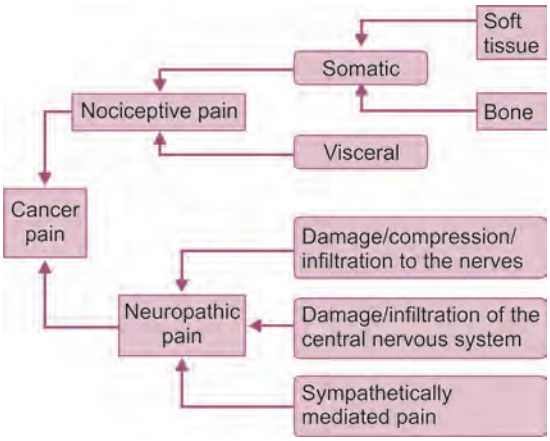


Fig. 27.2: Classification of cancer pain

remainder patients respectively.[3] Whereas the somatic nociceptive pain can be pin-pointed; the visceral nociceptive pain is poorly localized in nature. About one-third of cancer patients have mixed nociceptive-neuropathic pain or pure neuropathic pain. Pain descriptors like tingling, burning, electric shock like or stabbing are commonly used by patients to describe neuropathic pain. A number of questionnaires such as Neuropathic Pain Questionnaire, pain DETECT, Douleur Neuropathique[4] questions, ID pain and S-LANSS are available to assess neuropathic pain.

Cancer pain can also be classified based upon the severity of pain (numerical rating scale) into:

- Mild pain: 1–3,
- Moderate pain: 4–6 and
- Severe pain: 7–10.

Cancer patients frequently experience more than one site and type of pain. The pathophysiology and etiology of pain may be different at different sites in the same patient. Therefore, it is imperative to do a comprehensive assessment based upon patient's descriptors of pain, its characteristics and the significance imparted to it at all the sites of pain during the initial and each subsequent visit to ensure an effective pain management.[4] Understanding the pathophysiological mechanism of pain helps in selecting the appropriate analgesics, e.g. non-steroidal anti-inflammatory drugs (NSAIDs) and opioids for nociceptive pain and anticonvulsants or tricyclic antidepressants for neuropathic pain.

Breakthrough Pain

Breakthrough pain is a flare of pain against a background of adequate pain relief. It has the following characteristics:

- Rapid onset
- Short duration
- Moderate to severe in intensity.

It can be classified into:

Incident pain: Pain which occurs in response to a physical activity such as standing, walking, wound dressings, manual evacuation of feces.

Spontaneous pain: Pain which occurs in absence of any obvious provoking factor.

Therefore, when prescribing opioids (e.g. morphine) for cancer pain 10% of the total daily dose or the 4th hourly dose of morphine is prescribed as prn doses for the breakthrough pain.

Conclusion

Pain is one of the most common and distressing symptoms in cancer. Cancer pain is multifactorial in etiology, multi-dimensional in nature and may be mixed nociceptive-neuropathic in nature. Cancer patients may have pain at more than one site and the pathophysiology and nature of pain may be different at different sites in the same patient necessitating a comprehensive assessment and management.

REFERENCES

1. Van den Beuken-van Everdingen MHJ, de Rijke JM, Kessels AG, et al. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol. 2007; 18: 1437–49.
2. Dahl J. Implementing the JCAHO pain management standards. American Pain Society 19th Annual Meeting November 2–5, 2000, Atlanta, Georgia. Available from: http://www.medscape.com/viewarticle/420351
3. Zech DF, Grond S, Lynch J, et al. Validation of World Health Organization guidelines for cancer pain relief. Pain 1995;63:65–76.
4. Gupta M, Sahi MS, Bhargava AK, Talwar V. The prevalence and characteristics of pain in critically ill cancer patients: A prospective nonrandomized observational study. Indian J Palliat Care 2015;21:262–7.

CHAPTER

28

Pharmacotherapy in Cancer Pain

Sunny Malik and Gautam Das

INTRODUCTION

Cancer itself and pain associated with it significantly affects the quality of life and causes physical, psychological, emotional, social and spiritual trauma to the patient and family.

Cancer pain affects more than 9 million people worldwide annually[1]. Pain usually increases in severity as the cancer progresses towards a more complex and advanced stage. Majority of the emphasis in these patients is given for curative treatments inclusive of radiotherapy, chemotherapy and/or surgery with a little emphasis upon pain management. This undertreated problem of cancer pain can be easily solved via a comprehensive approach using pharmacotherapy alone or in combination with interventional pain management. The management of cancer pain is usually multimodal in nature comprising of non-pharmacological, pharmacological and interventional pain management techniques. This chapter focuses on analgesics used in cancer pain management and how to prescribe them.

WHO Analgesic Ladder

Pharmacotherapy constitutes the mainstay of cancer pain management. The World Health Organization (WHO) in 1986 proposed the three step analgesic ladder for cancer pain management.

Step I: Mild to moderate pain → **Non-opioids** such as acetaminophen/NSAIDs ± Adjuvants.

Step II: Moderate to severe pain → Step I ± **weak opioids** like tramadol/codeine.

Step III: Severe pain → Step I ± strong opioids morphine/fentanyl.

Step IV (modification): Interventional pain management.

Adjuvants include laxatives, anti-emetics, and co-analgesics, etc. (Fig. 28.1)

The essential concepts of WHO stepladder approach comprises:

- By the mouth (most preferred route),
- By the clock,

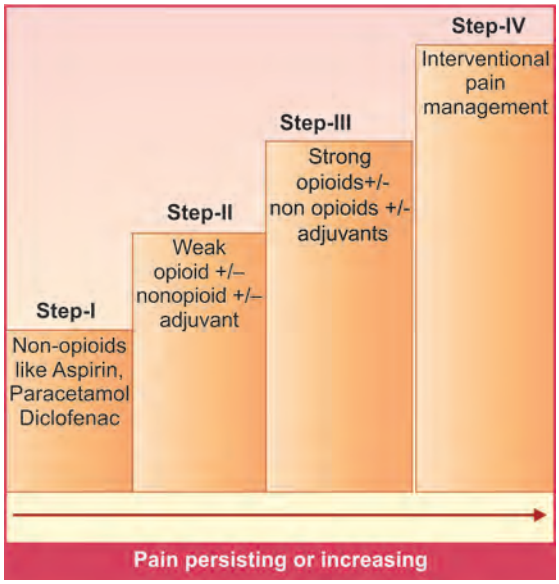


Fig. 28.1: WHO analgesic ladder

- By the ladder and
- For the individual (dose tailored to the need).

Acetaminophen is used for mild to moderate pain and has minimal anti-inflammatory properties. Non opioids like acetaminophen are usually co-prescribed with opioids because of their opioid sparing effects. They are weak analgesics prescribed as 1 gram dose thrice daily. The total daily dose should not exceed 4 grams per day. Caution is required in patients with chronic alcoholism and hepatic failure.[2]

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

They are useful in inflammatory nociceptive pain like bone metastasis.[2,3] NSAIDs can be used as monotherapy for mild pain or in combination with opioids for moderate-severe pain. NSAIDs are non selective COX inhibitor used for cancer pain, but may be associated with side effects such as nephrotoxicity, gastrointestinal bleeding and peripheral edema. They should be used with caution in patients with history of allergy and asthma as they can induce bronchospasm in about 20 % of subjects.[4,5] Newer selective COX-2 inhibitors are in use recently due to their comparable side-effect profile. But caution is required in patients with history of stroke, myocardial infarction and cardiovascular or cerebrovascular risk factors.

Opioids

Before going into details of common opioids used for cancer pain, a clear understanding of certain common terms used with cancer pain management is necessary.

Step up Step Down

It is bidirectional way of using the WHO step ladder.[11] With increasing or persisting pain it is advisable to move to the next step (e.g. step I to Step II or Step II to Step III) and the reverse that is descending to a lower step with decreasing pain intensity (e.g. after the tumor has responded to the curative treatments or after interventional pain therapy).

Scheduling and Titration of Dose

Start with a low dose in opioid naïve patients (e.g. 5 mg q4h and pm) with frequent follow-ups for effect and any associated side-effect. If patients require more than two breakthrough doses, the daily dose is increased either by 25% or by dividing the total daily dose of morphine consumed over the previous day (sum of all 4 hourly doses and breakthrough doses) into 6 equal doses. Now the new 4th hourly dose is prescribed pm for the breakthrough pain.

Opioid Rotation

Opioid rotation refers to switching from one opioid to another either to improve the analgesic effect or to reduce the adverse effects of the opioid therapy or both. Opioid rotation works owing to varying affinity of different opioids to different opioid receptors and inter individual variation in response of patients to different opioids. The principles behind opioid rotation are empirical at best and done by using commonly available equi-analgesic dose conversion tables.

Concept of Breakthrough Pain (BTP)

It is flare of pain against a background of adequate pain relief. It typically lasts for 30–45 minutes and managed by prescribing PRN dose of fast acting opioid like immediate release morphine in addition to the regular doses. Oral immediate release morphine equivalent to 10% of the daily dose or the 4th hourly dose is prescribed pm for the breakthrough pain. Trans mucosal fentanyl, intravenous morphine or subcutaneous morphine might also be of help. It has been found that patient's age, gender and the duration of pain shows no relationship with BTP.

Common opioids in use for cancer pain are given in Table 28.1. [3, 6–8]

Table 28.1: Common opioids in use for cancer pain

Tramadol (weak opioid)	*Morphine (strong opioid)*	*Fentanyl*	*Buprenorphine*
Mild to moderate pain **MOA:** 1. μ-receptor agonist. Lesser extent: δ and κ receptors too. 2. Activates spinal inhibition of pain due to decreased reuptake of norepinephrine and serotonin. One-fifth to one-tenth potent than morphine **Routes:** Oral, intravenous, intra-articular, neuraxial **Dose:** 50–100 mg PO TDS-QID, not to exceed 400 mg per day. Tramadol extended release tablets: 100 mg once daily titrated up by 100 mg increments every 5 days, but not to exceed 300 mg per day. **Side effects:** Seizure, sedation, emesis, itching, dizziness, high serotonin levels causing agitation, raised HR, vomiting, diarrhea, fainting, loss of co-ordination, etc.	Moderate to severe pain **MOA:** Acts directly on CNS **Routes:** Oral, sublingual, buccal, intravenous, epidural, intrathecal, rectal. Parenteral dose 1/3rd–1/4th of oral dose. **Dose:** 5 mg 4th hourly and pm. Increase the dose by about 25–30 % if more than 2 breakthrough doses required over previous 24 hours. Switch to sustained and extended release formulations once pain is controlled. **Side effects:** Constipation, pruritus, bradycardia, histamine release, drowsiness, nausea, vomiting, dependence, miosis, respiratory depression. Caution needed in patients with asthma, hyper-reactive airways and renal failure. **Naloxone** is the antidote.	Moderate to severe pain **MOA:** Synthetic opioid, μ-receptor agonist. 80–100 times **more potent** than morphine. **Routes:** Oral, transdermal, buccal, I/M, I/V, epidural, intrathecal. **Dose:**Transdermal patches are recently available in the form of 25, 50, 75 or 100 micrograms/hour patch. Effect of patch starts only after 12–18 hours on first application due to build up of steady plasma concentration. Patch works for 3 days. Concentration of fentanyl decreases in 12–18 hours post patch removal. But, it cannot be used if rapid analgesia is required. Not to be used in opioid naïve patients. **Fentanyl lollipops (OTFC)** are faster acting by transmucosal absorption. They are berry flavoured lozenges, to beput inside the mouth (inside of the cheeks, on and under the gums and tongue). It is to be consumed fast within 15 minutes. Useful for breakthrough pain. About 25% of this drug is absorbed quickly via oral mucosa and rest is swallowed to be absorbed from the small intestine. Recently, a fentanyl patient controlled transdermal system (PCTS) is under development. **Side effects:** Nausea, somnolence, confusion, constipation, **chest rigidity**, dyspnoea, hypoventilation.	Moderate to severe pain **MOA:** Partial μ-receptor opioid agonist. Have a longer duration of action. **Routes:** Sublingual tablets, injection solution, transdermal patch **Dose:** Transdermal patch is readily available. 5/10/20 micrograms per hour release patches are available. 7days preparation is available. Analgesic effect starts from 3rd day. **Side effects:** Blurred vision, cough, nausea, confusion, pinpoint pupils, dizziness, pale/blue lips and nails, shortness of breath.

Table 28.2: Opioid equivalent doses[9]

Drug name	Drug dose	Equivalent oral morphine dose
Codeine	30 mg	4.5 mg
Dihydrocodeine	10 mg	1 mg
Tramadol	50 mg	5 to 10 mg
Drug name Buprenorphine patch	**Equivalent codeine dose**	**Equivalent oral morphine dose**
BuTrans 5: 5 µg/hr	60 mg/24 hrs	10 mg/24 hrs
BuTrans 10: 10 µg/hr	120 mg/24 hrs	20 mg/24 hrs
BuTrans 20:20 µg/hr	240 mg/24 hrs	40 mg/24 hrs
Drug name fentanyl patch		**Equivalent oral morphine dose**
Fentanyl 25: 25 µg/hr		30 to 134 mg/24 hrs
Fentanyl 50: 50 µg/hr		135 to 224 mg/24 hrs
Fentanyl 75: 75 µg/hr		225 to 314 mg/24 hrs
Fentanyl 100: 100 µg/hr		315 to 404 mg/24 hrs

Adjuvants

Adjuvants are drugs which are primarily indicated in conditions other than pain but have some analgesic properties. They can be combined with opioids at any step of the WHO stepladder. The frequently prescribed ones include antidepressants, anticonvulsants, NMDA antagonists, α-2 agonists, muscle relaxants, calcitonin and bisphosphonates. Common adjuvants used in cancer pain pharmacotherapy are tabulated in Table 28.3. [2, 3]

Table 28.3: Common adjuvants used in cancer pain pharmacotherapy

Drug class	*MOA*	*Dose*	*Side effects*
Antidepressants Tricyclics	Serotonin and norepinephrine reuptake inhibition	**Amitriptyline/ Nortryptiline/ Desipramine** 10–25 mg/day (max dose 150 mg/day)	**Anticholinergic side effects:** Xerostomia, xerophthalmia, urinary retention, blurred vision, constipation, sedation, cardiac arrhythmias, orthostatic hypotension, sleep disruption. Less with nortryptiline.
Antidepressants	Selective serotonin norepinephrine reuptake inhibitors	**Duloxetine** 20–30 mg/ day (max dose 120 mg/day) **Milnacipran** 25 mg BD (max dose 200 mg/day) **Venlafaxine** 25 mg BD (max dose 300–400 mg/day)	**Lesser than tricyclics.** Nausea, hyperhidrosis, dry mouth, sexual dysfunction, constipation, somnolence
Anticonvulsants Carbamazepine (for neuralgia) **Anticonvulsant Gabapentin**	Modulate voltage-dependent sodium channels Blocks analogue of GABA α-2 δ-subunit of the voltage-dependent calcium channel and thus reducing the influx of calcium into the nerve endings	100 mg/day (max dose 1200 mg/day) 100 mg thrice daily (max dose 3600 mg/day)	Liver dysfunction, aplastic anemia. **Somnolence, dizziness, weight gain**, loss of co-ordination

Contd.

Table 28.3: Common adjuvants used in cancer pain pharmacotherapy (Contd.)

Drug class	*MOA*	*Dose*	*Side effects*
Pregabalin		75 mg/day (max dose 300 mg/day)	**Hypotension, bradycardia, AV block**, somnolence, dizziness,
α-2 agonists Clonidine Tizanidine	Pre-synaptically decrease neurotransmitter release Postsynaptically hyperpolarize neurons—less likely to fire **Sympatholytic effect**	Clonidine epidurally (0.5–30 microgram/kg /hour) along with opioids given for severe cancer pain. Not to exceed 40 microgram /kg/hour. It is effective in neuropathic pain. **Tizanidine is α-2 selective anti-spasticity agent.**	Dry mouth, headache, erectile dysfunction
NMDA antagonists Ketamine	NMDA receptor blocker thus preventing increased pain sensitivity due to Wind-up **Reduce hyperalgesia and central sensitization**	A slow bolus of 0.25–0.5 mg/kg in sub-hypnotic doses improves opioid analgesia in difficult pain syndromes of neuropathic pain	**Hallucinations, sympathomimetic effects**, raised ICP, increased bronchial secretions, **nystagmus**, double vision, **emergence reaction**
Steroid Triamcinolone Methylprednisolone Betamethasone Dexamethasone Deflazacort	Reduce inflammation: Inhibit phospholipase A2 Blocks transmission of nociceptive C fiber Input, thus suppresses ongoing and ectopic neural discharge	Dexamethasone (common) PO/IV: 10–20 mg every 6 hours. **Low dose regime** (advanced disease with daily pain): Dexamethasone 2–4 mg OD/BD. Last dose not beyond 4 pm. **High dose regime** (spinal cord compression/ acute severe pain): 100 mg, followed initially by 96 mg/ day in divided doses. Prednisone 40–100 mg PO. **Interventions with depot steroid** 3 mg/kg/year 6 mg/kg/lifetime	Immunosuppression, hyperglycemia, myopathy, peptic ulceration, osteoporosis, Cushing's syndrome

Miscellaneous

Bone Pain

NSAIDs, corticosteroids, bisphosphonates, and the radiopharmaceuticals.

Strontium chloride (89Sr) and 153Sm-lexidronan are used for intractable bone pain. **Bisphosphonates** such as pamidronate and zolendronate have been proved efficacious in reducing skeletal complications and pain from bone metastases.[10] Calcitonin used previously is nowadays not a favourite alternative in bone pain.

Baclofen

An agonist at GABA-B type receptor, quite efficacious in trigeminal neuralgia is nowadays considered in neuropathic pain. The effective dose ranges from 20 to 200 mg/day orally. It is gradually tapered off to prevent withdrawal

symptoms. It is also used in treatment of spasticity and central pain secondary to spinal cord lesions.[3, 11]

Lastly, **topical agents** are also available for cutaneous application in areas of hyperalgesia and hyperesthesia such as lidocaine patches, capsaicin ointment and EMLA cream (Eutectic mixture 2.5% lidocaine + 2.5% prilocaine). Even extended application of lidocaine patches has been tried for up to 24 hours/day for up to 4 days with minimal systemic absorption in healthy volunteers and post-herpetic neuralgia patients.[3]

To conclude primary cancer pain management depends on proper assessment, opioids availability, dose titration via reassessment and appropriate use of co-analgesics.

REFERENCES

1. Ripamonti C. Cancer pain syndromes and pharmacotherapy of cancer pain. Arch Oncol 2004; 12 (3): 168–70.
2. Blinderman CD. Management of cancer pain: Optimal pharmacotherapy and the role of interventions. Adv Pain Manage. 2008; 1(4):122–40.
3. Gehdoo RP. Cancer Pain Management. Indian J Anaesth. 2006;50(5):375–90.
4. McQuay HJ, Moore A. Non-opioid analgesics. In: Doyle D, Hanks G, Cherny N, Calman K, editors. Oxford Textbook of Palliative Medicine, 3rd ed. Oxford, UK: Oxford University Press, 2005:348.
5. Abrahm JL. Advances in pain management for older adult patients. Clin Geriatr Med 2000; 16:269–311.
6. Leppert W. Tramadol as an analgesic for mild to moderate cancer pain. Pharmacological reports. 2009;61(6):978–92.
7. Fukuda K. Opioid Analgesics. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anesthesia. 8th ed. The United States of America: Elsevier; 2010. P 864–915.
8. Stoelting RK, Hillier SC. Section I- Opioid Agonists and Antagonists In: Stoelting RK, Hillier SC, editors. Pharmacology and Physiology in Anesthetic Practice. 4th ed. Philadelphia: Walters Kluwer Company. P 87–126.
9. http://www.wales.nhs.uk/sites3/Documents/814/Opioid In Non-malignant Pain %2 DGwent Guidance %5 B Final %5 D Jan2010. pdf.
10. Cascinu S, Graziano F, Alessandroni P et al. Different doses of pamidronate in patients with painful osteolytic bone metastases. Support Care Cancer 1998;6:139–43.
11. Fromm GH. Baclofen as an adjuvant analgesic. J Pain Symptom Manage 1994; 9: 500–9.

CHAPTER

29

Interventions in Cancer Pain

Gautam Das and Mousumi Datta

INTRODUCTION

Majority (70–90%) of patients with cancer pain get adequate pain relief with the World Health Organization's three-step analgesic ladder. However, some 10–30% of patients may either fail to obtain adequate pain relief or develop intractable side-effects with the pharmacological management. The interventional pain management techniques was added as the fourth step to the WHO analgesic ladder to address pain issues in such patients. Certain pain interventions such as celiac plexus neurolysis may even have a role early in the management of cancer pain as they have been shown to provide better analgesia and improved quality of life.[2] In present scenario interventions form an integral part in providing pain relief in complex cancer pains.[3] Interventions can be added at any step of management of cancer pain depending on type and severity of pain. Though in individual patients the risk: benefit ratio should be considered before implementing invasive analgesic methods.

Fourth Step in WHO Analgesic Ladder[1,2]

The new fourth step in WHO ladder is recommended for the treatment of those patients who have failed oral or transdermal options. Failure may be due to the inability to achieve adequate pain relief or the development of undesirable/intolerable side effects such as sedation, nausea/vomiting, constipation, and confusion. This fourth step is "interventional" and includes the use of nerve blocks, spinal (epidural and subarachnoid) administration of local anesthetics, opioids, α-2 agonists, spinal cord stimulation, and surgical interventions as required according to patient's condition (Fig. 29.1).

Indication for Intervention[4,5]

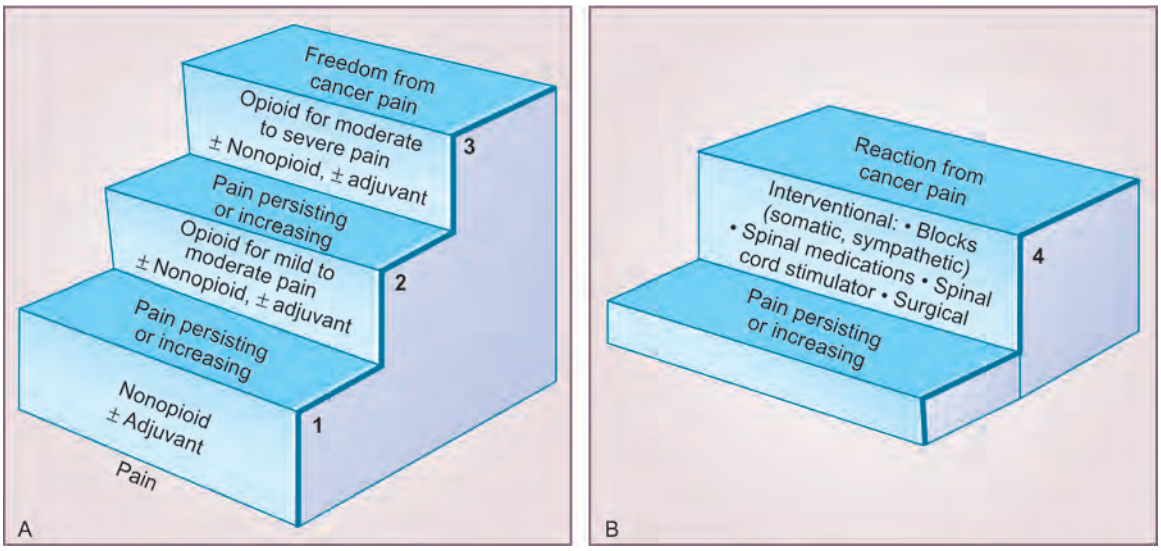
- When a comprehensive trial of pharmacologic therapy fails to provide adequate analgesia
- Unacceptable side effects
- Well localised pain syndromes: Pain likely to be relieved by nerve blocks.

Interventional techniques for pain management can be classified into:[3]

- Regional infusions
- Including intrathecal pump
- Neuraxial analgesia
- Neurodestructive procedures
- Neuromodulation
- Percutaneous vertebroplasty/kyphoplasty/Cementoplasty
- Radiofrequency ablation

INTERVENTIONAL PAIN MANAGEMENT TECHNIQUES: A BRIEF OVERVIEW[3,5,6]

- **Continuous Subcutaneous Infusion of Opioids:** Useful in palliative care settings in patients unable to accept orally.
- **Intravenous Infusion of Opioids with Patient-Controlled Analgesia Devices:** Indicated in severe pain where oral route


Freedom from cancer pain
Opioid for moderate to severe pain ± Nonopioid, ± adjuvant
3
Pain persisting or increasing
Opioid for mild to moderate pain ± Nonopioid, ± adjuvant
2
Pain persisting or increasing
Nonopioid ± Adjuvant
1
Pain
A
Reaction from cancer pain
Interventional: • Blocks (somatic, sympathetic) • Spinal medications • Spinal cord stimulator • Surgical
4
Pain persisting or increasing
B

Figs 29.1 A and B: (A) The 3-step analgesic ladder developed by the World Health Organization. Reproduced by permission of WHO. Cancer Pain relief. Gebeva: WHO; 1986; (B) proposed 4th step

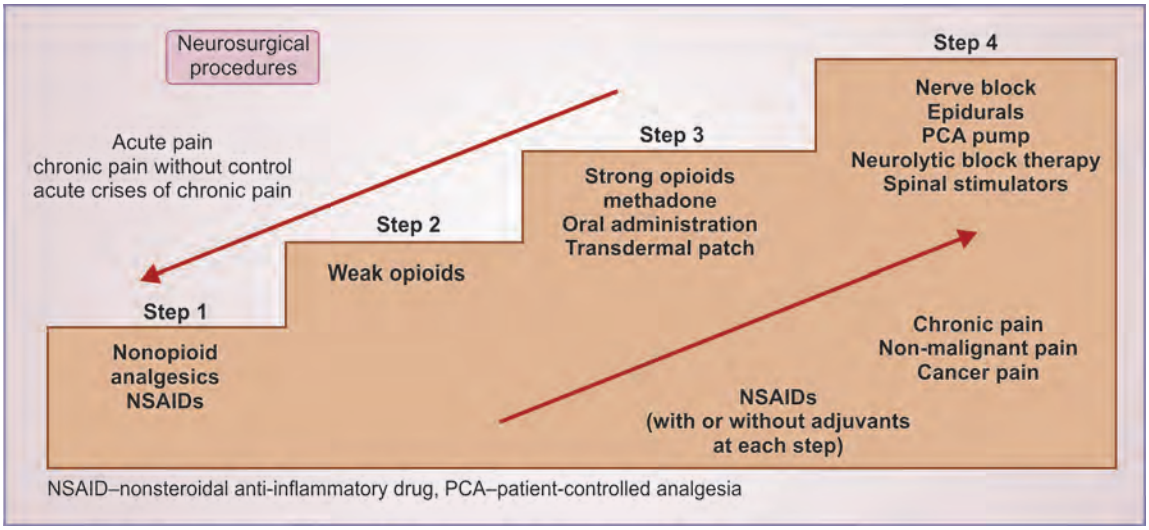


Fig. 29.2: New adaptation of the analgesic ladder

is not available. Though pain relief is satisfactory in most cases, this needs a controlled environment where monitoring can be done. It is mostly useful in hospital settings in admitted patients.

- **Intraspinal Analgesia:** Neuraxial analgesia is achieved by the epidural or intrathecal administration of an opioid alone (very rarely) or in combination with other agents such as bupivacaine, clonidine, or ziconotide. In general patient's life expectancy should be more than three months. Major disadvantage is the cost of the devices.
- **Nerve Blocks:** Local anesthetic injections can be used for diagnostic or therapeutic purposes, or both. This helps the clinician determine the potential for subsequent neurolysis, if needed.

- **Neurolytic Procedures:** Ablation of pain carrying nerve for pain relief is known as neurolysis. Neurolysis offers long-term pain relief and need of opioid are reduced. Alcohol and phenol are the two agents commonly used to produce chemical neurolysis. Apart from chemical neurolysis, radiofrequency neurolysis and cryo-neurolysis are other two popular option for neurolysis. Common neurolytic procedure are celiac plexus block in patients with upper GI carcinoma, superior hypogastric plexus neurolysis in pelvic malignancy.
- **Peripheral and Cranial Nerve Blocks:** Blockade of the ganglion of Gasser, within the foramen ovale at the base of skull or its branches, may be beneficial for pain in the distribution of trigeminal nerve. Though indications in tumor-related pain are minimal, because of the neuropathic component.
- **Vertebroplasty:** Percutaneous vertebroplasty (PV) is a minimally invasive procedure involving the injection of bone cement (usually polymethylmethacrylate [PMMA]) into the fractured vertebral body to alleviate the pain and give some structural stability.
- **Spinal Cord Stimulation:** May be used for refractory neuropathic chronic pain, though patient selection is important in the cancer population, because MRI at this point is contraindicated after the device is placed.
- **Neurosurgical Palliative Techniques:** For example, Percutaneous cordotomy produces a thermal lesion in the substance of the spinal cord and reliably relieves unilateral truncal and lower limb pain. We shall discuss some important interventional procedures for cancer pain management.

INTRATHECAL PUMP

Introduction: Intrathecal pump is one most useful option of cancer pain management. When opioid like morphine is injected into the intrathecal space the dose is reduced very much. For morphine, 300 mg of oral morphine is equivalent to 1 mg of intrathecal morphine. Thus, intrathecal morphine provides much superior analgesia with minimal adverse reaction of morphine.

Patient selection:

1. Patient have severe pain.
2. Life expectancy is more than 3 months.
3. Multiple area pain can not be covered adequately with neurolysis.
4. Patient have adequate pain relief with opioid.
5. Patient does not have any major psychological issues.

Test dose: Before selecting patient for intrathecal drug delivery system, a test dose of the opioid in given in intrathecal or epidural route. Most commonly 0.5 mg of morphine is injected as test dose if patient is not on any opioid. If patient is on some opioid, a higher dose can be given. If patient enjoys good pain relief, intrathecal pump may be implanted.

Procedure: The procedure is done under C-arm guidance. Radio-opaque catheter is placed at mid-thoracic area and the reservoir is implanted in a subcutaneous pocket in subcostal area. The reservoir capacity is between 30–60 ml and flow of drug is between 0.5–1 ml/24 hours.

There are two types of pumps. One of them is mechanical pump which is fixed flow pump. Here, the flow is fixed, no battery is needed. Other one is battery operated pump where flow can be changed with remote operated from outside the body. Mechanical pump is less costly and have longed life than battery operated pumps, but have the disadvantage of fixed rate of drug delivery.

CELIAC PLEXUS BLOCK

Introduction: Celiac plexus neurolysis is one of the most commonly done neurolytic blocks done in cancer patients. It has very high success rate and several studies recommend

that it can be a preferred option of pain management than pharmacotherapy is pancreatic cancer even in early stage.

Patient selection:

1. Moderate to severe pain localized in epigastrium with or without referred pain in back due to upper abdominal malignancy.
2. There should be no coagulopathy.
3. No distal painful metastasis.
4. More than few months of life expectation.

Diagnostic block: Diagnostic block is controversial in cancer patients. Some prefer to go directly for neurolytic procedure without a diagnostic block, some looks for pain relief after local anaesthetic injection on same sitting while some wait for the results of diagnostic block and prefer to do it on subsequent days. Thus, in cancer pain management, diagnostic block is not mandatory before this neurolytic procedure.

Procedure: The procedure can be done under ultrasound (USG) guidance, CT guidance or under C-arm guidance. It can be done from anterior approach or, posterior approach.

USG guided procedure have the advantage of doing procedure at bedside, no need of placing patient in prone, no radiation exposure. Disadvantage of USG guided procedure is non-visualization of target in poorly bowel-prepared patients. Celiac artery is identified where it is divided into splenic artery and hepatic artery.

C-arm guided procedures are done with the patient is prone. Needle is placed at L1 level in front of aorta. After confirming needle position with dye injection, 20–25 ml of alcohol is injected on either side. Single needle placement is enough if needle is placed through aorta which is called transaortic approach.

HYPOGASTRIC PLEXUS BLOCK

Introduction: This is another commonly done intervention for cancer pain. Like celiac plexus block in upper abdominal malignancy, this procedure is also preferred over pharmacotherapy in moderate to severe pain because of pelvic malignancy.

Patient selection

1. Moderate to severe pain in lower abdomen and pelvis due to malignancy.
2. Pain localizes in lower abdomen, pelvis and lower back.
3. No distal painful metastasis
4. Life expectancy is more than few months.

Like celiac plexus block, diagnostic block is not mandatory in cancer pain management.

Procedure: This procedure can be done both under USG or C-arm guidance. Like celiac plexus block, this neurolytic procedure is also preferably done under USG guidance. Under USG guidance, the patient remains in supine position and the bifurcation of aorta is identified. Approximately 15 cc of alcohol or phenol is injected after local anaesthetic injection when alcohol is used.

Patient is place prone when it is done under C-arm guidance. The needle is placed at anterolateral aspect of L5-S1 vertebral body. Some prefers trans-discal approach to reach the target.

CEMENTOPLASTY

Introduction: Bone metastasis is an extreme painful condition in cancer patients. Pain of bone metastasis can be managed with radiotherapy, bisphosphonates and also by cementoplasty. It is a procedure where liquid bone cement is injected at metastatic site under C-arm guidance. Depending on the site of injection, it has different names, like vertebroplasty, sacroplas.

Conclusion

Interventional pain management is indicated in select few cancer patients who either fail to achieve inadequate pain relief or develop intractable side-effects with the pharmacological techniques. Early institution may be indicated in a minority of patients such as celiac plexus

block for patients with Ca pancreas which has been shown to provide adequate analgesia as well as improve QoL and even survival. The interventions are usually best suited for well localized pain and only after addressing risk-benefit in in individual patients. The complexity involved and the risk of serious life-threatening adverse effects necessitates proper patient selection and interventions being performed by qualified and experienced interventional pain physicians in a well equipped infrastructure.

REFERENCES

1. Miguel R. Interventional treatment of cancer pain: the fourth step in the World Health Organization analgesic ladder? Cancer Control. 2000;7(2): 149–56.
2. Vargas-Schaffer G. Is the WHO analgesic ladder still valid? Twenty-four years of experience. Can Fam Physician. 2010;56 (6):514–7.
3. Oscar de Leon-Casasola, Yarussi A. Cancer Pain. In: Honorio T. Benzon et al. editors. Raj's practical management of pain. 4th ed. Philadelphia: Mosby Elsevier; 2008.p. 413–426.
4. The British Pain Society. Invasive procedures for cancer pain. In: The British Pain Society's Cancer Pain Management. London: The British Pain Society; 2010.p. 63–72.
5. National Comprehensive Cancer Network (NCCN). Adult cancer pain. NCCN Guidelines Version 1. 2014.
6. Joshi M. Cancer pain. In: Joshi M editor. Textbook of pain management. 3rd ed. Hyderabad: Paras: 2014.p.392–405.
7. Thomas E, Weiss S: Non-pharmacological interventions with chronic cancer pain in adults. Cancer Control. 2000;7(2):157–164.

CHAPTER

30

Palliative Care in Cancer

Mayank Gupta and Abdulkafi Alsaied

India like most other countries in the world is experiencing a health transition with the majority of the disease burden and the death being attributable to the non-communicable diseases like cancer, chronic heart, kidney, respiratory and neurological diseases. **Chronic diseases** account for an approximately 53% and 66% of all deaths in India and world respectively.

In India approximately 1 million new cases of **cancer** are diagnosed each year with the prevalence estimated at around 4 million. These patients suffer from a very **high symptom burden** like pain, breathlessness, nausea, constipation and delirium, etc. Over 70% of these present in stage III and IV when the curative treatments are much less effective and palliative care plays a dominant role. With the modern healthcare practice being inclined towards curative treatments and lack of acknowledgement of palliative care among both the general public and the healthcare professionals; this suffering goes largely unheard.

What is Palliative Care?

Palliative care is an approach that improves the **quality of life** of **patients and their families** facing the problem associated with **life-threatening illness**, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems (including) physical, psychosocial and spiritual.[1]

The three pillars of palliative care as shown in Fig. 30.1 are[2]:

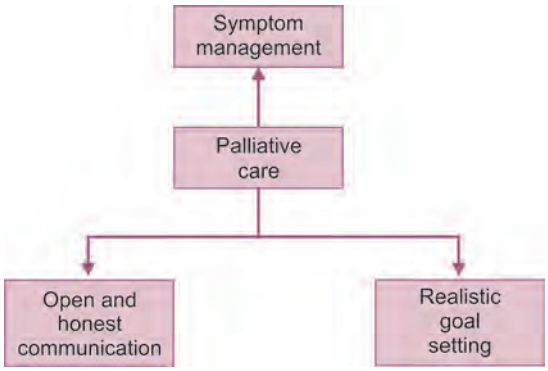


Fig. 30.1: Pillars of palliative care

Principles of Palliative Care

Palliative Care in Cancer

- Is **symptom and illness oriented** rather than disease oriented.
- Affirms life and regards dying as a normal process;
- Intends neither to hasten or postpone death;
- Integrates the **psychological and spiritual aspects** of patient care;
- Offers a **support system** to help patient's live as actively as possible until death;
- Offers a **support system to help the family** cope during the patients illness

(patient's illness) and in their own bereavement;

- Uses a **team approach** to address the needs of patients and their families, including bereavement counselling, if indicated;
- Is applicable **early in the course of illness**, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications (Fig. 30.2).

Palliative care for children is the active total care of the child's body, mind and spirit, and also involves giving support to the family.

Worldwide 20.4 million people, out of whom 6% are children and 78% are concentrated in low-middle income countries, require palliative care.[3] The **need of palliative care** in(for) cancer in India alone is estimated to be around 4 million but <4% have access to palliative care with < 2% having access to essential medications for pain and symptom control.[4] Palliative care has been declared as a "**Fundamental Human Right**" and the **World Health Assembly** passed a resolution in 2014 urging all the countries to integrate palliative care into all healthcare services, policy development and education. At present there are approximately 247 palliative care services in India out of which 75% are concentrated in Kerala.

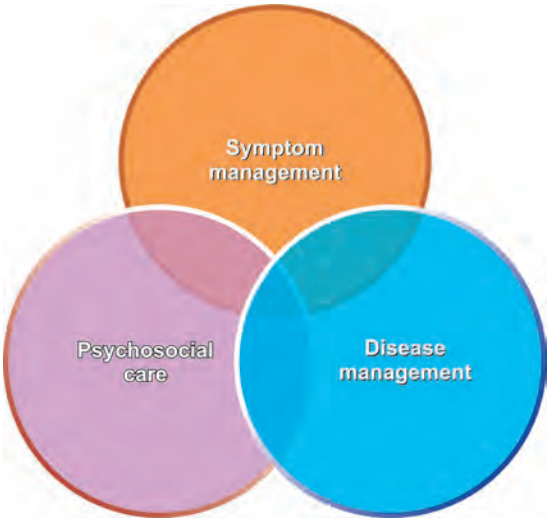


Fig. 30.2: The interconnected domains of palliative care

Diseases in Need of Palliative Care

All chronic life-limiting illness like Cancer, HIV/AIDS, kidney failure, heart failure, chronic obstructive pulmonary disease, dementia, motor neuron disease, multiple sclerosis, cirrhosis, Parkinson's disease, etc.[3] The philosophy of palliative care advocates its provision **irrespective of the diagnosis, prognosis and stage of the disease**. **Supportive care** is a broader term that encompasses applying all the principles of palliative care starting from the time of diagnosis alongside disease specific treatment in chronic ailments like cancer. As the disease progresses and the curative treatments decreases, the role of palliative care increases. At the end of life, palliative care is provided as **terminal care** extending as bereavement counseling and support for grieving family after the patient's death (Fig. 30.3). **'Hospice care'** is supporting patients at the end of life (last 6 months of life) to allow them to die in comfort and with dignity. After the death of the patient, palliative care is provided as the bereavement care to the grieving family.[5]

What Are the Benefits of Palliative Care?

The benefits are both clinical and financial.[2] Delivery of palliative care simultaneously with the curative treatments improves symptoms not only due to the disease but also due to the treatment; thereby improving the tolerance to mutilating treatments like chemotherapy or radiotherapy. It improves the quality of life and death by goal setting, respecting the patient's choice of place of death and type of care and hence avoiding the futile interventions in the end. It is economical both for the patients and the hospitals by diverting the terminal care from the hospitals to the home care settings and

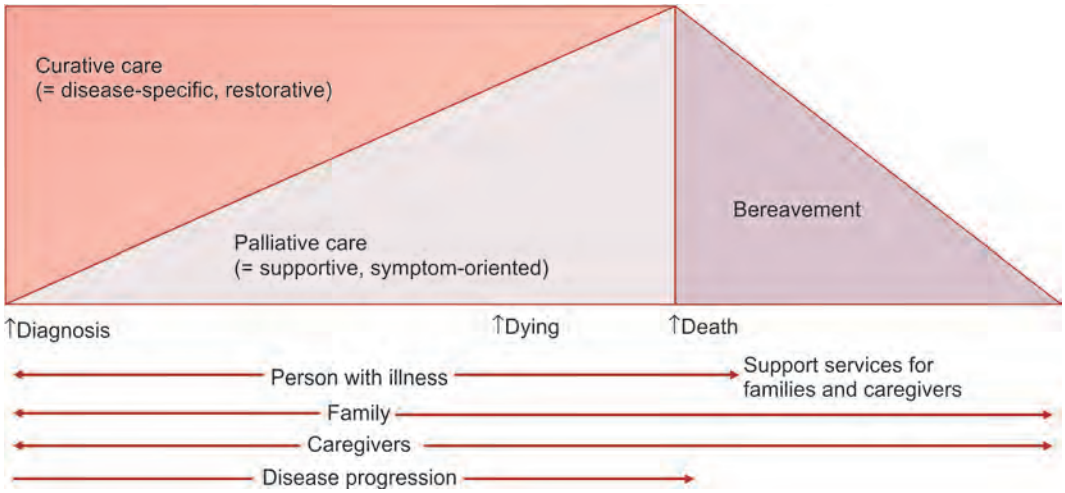


Fig. 30.3: Continuum of palliative care

ensuring the availability of the costly hospital beds to those in need of acute care.

Spectrum of palliative care services includes[2]:

1. ***Outpatient clinics*** (OPD): Easy to establish with minimal infrastructure (reallocation or sharing of the available resources) and at low cost.
2. ***Inpatient consultation services***: For hospital inpatients in need of palliative care.
3. ***Day care services*** including respite care
4. ***Inpatient palliative care unit with or without consultation services:*** For patients with severe symptomatic distress (e.g. severe pain in need of intravenous morphine titration), terminal care and patients in need of procedures like interventional pain management, ascitic tap, pleurodesis, etc.
5. ***Home care services***: Forms the crux of palliative care services.

Depending upon the manpower and infrastructure available, one may start from an **outpatient service** and may later on incorporate others like inpatient consultation services, a dedicated inpatient palliative care unit and home care services into their spectrum of services.

Who Can Deliver Palliative Care?

Palliative care is an interdisciplinary team effort with the team consisting of doctors, nurses, physiotherapists, psychologists, social workers, chaplains, pharmacists and last but not the least volunteers. However, it is not mandatory to have a full team to start palliative care services. One may start up the services (usually doctors) and may slowly build on the team as required. Palliative care is a new medical specialty in India with MD Palliative medicine being already offered by two medical institutes (Tata Memorial Hospital and the All India Institute of Medical Sciences, New Delhi). A number of certificate courses (like the **Certificate course in essentials of palliative care** by the **Indian Association of Palliative Care**) and fellowships (like the one year fellowship in palliative medicine by the institute of palliative medicine) are also available for doctors and nurses from a number of organizations and institutes working actively in the field of palliative care.

Conclusion

Palliative care aims to improve the quality of life of patients and their families suffering from chronic life-limiting illness. Effective

symptom management, open communication and realistic goal setting are the main pillars of palliative care. It is a fundamental human right to be available irrespective of the diagnosis or stage but to all those who need it; ideally as soon as the diagnosis is made. The benefits of the same are both clinical and economical.

REFERENCES

1. WHO Definition of Palliative Care. Available at: www.who.int/cancer/palliative/definition/en
2. Smith TJ, Coyne PJ, Cassel JB. Practical guidelines for developing new palliative care services: resource management. Annals of Oncology 2012;23 (Supplement 3): iii70–iii75.
3. Connor S, Bermedo MC. Global atlas of palliative care at the End of life. World Palliative Care Alliance. World Health Organization; 2014.
4. http://censusindia.gov.in/vital_statistics/SRS_Bulletins/SRS_Bulletin-September_2013.pdf.
5. Definition of Hospice. Medline Plus. Available at: www. nlm.nih.gov/medlineplus/hospicecare.html.

CHAPTER

31

Myths in Cancer Pain

Mayank Gupta

Myths, misconceptions, lack of knowledge and education are the main culprits identified behind the inadequate cancer pain management. The aim of this chapter is to demystify some of the common prevailing myths about cancer pain and its management.

Myth#1 Pain is an inevitable part and parcel of cancer.

Fact#1 Not all cancer patients have pain. An estimated **50–70%** and up to **80–90%** of patients with cancer and advanced cancer respectively suffer from pain with more than one-third of patients having moderate to severe pain.[1] Pain can be **effectively controlled** in 70–80% of patients by the use of oral pharmacological agents as per the WHO analgesic ladder.[2]

Myth#2 All pain in cancer patients are pain due to cancer.

Fact#2 Pain in cancer patients may be due to **cancer** (infiltration/compression, etc), **treatment** (phantom limb pain, chemotherapy induced neuropathic pain, etc.), **debility** (pressure sore) or **co-morbid conditions** (arthritis, low back pain etc).[3,4] The cause of pain at different sites may be different in the same patient. A comprehensive and unbiased assessment is required to diagnose the exact cause of pain in a particular patient. Understanding the etiology of pain is of utmost importance for effective pain management as the first principle of symptom management is "**Treat the treatable cause**".

Myth#3 Analgesics should be taken on SOS basis when pain is intolerable as their regular use may lead to addiction.

Fact#3 ***Analgesics for chronic pain should be prescribed on round the clock basis*** with a provision for breakthrough pain and not on SOS basis.[5] Prescribing on SOS basis may lead to peak and through effect and suboptimal pain management which can have many adverse consequences like depression, sleep disturbance, feeling of helplessness and despair, etc. Irrational opiophobia is one of the main reasons behind inadequate pain management. Use of opioids has not been found to be associated with either physical dependence or addiction.[6,7]

Myth#4 Morphine is the panacea for all cancer pains.

Fact#4 Analgesics for cancer pain are prescribed according to the intensity (mild, moderate or severe) and the type (nociceptive or neuropathic) of pain. Morphine is usually reserved for severe nociceptive pain and neuropathic pain is only partially responsive to opioids.[8] Since the cancer pain is multifaceted; a single analgesic may not be adequate to alleviate all the pains.[7]

Myth #5 Use of morphine causes respiratory depression and may hasten death.

Fact#5 Pain is a physiological antagonist to respiratory depression. Rational use of morphine in patients for cancer pain has been found to be safe and effective.[9] However, in elderly patients, patients with impaired

cardiopulmonary status, hepatic or renal failure doses may need to be adjusted either by reducing the dose or increasing the time interval between subsequent doses.

Myth#6 Morphine should be used as a last resort.

Fact#6 Morphine is considered as the wonder drug and "gold standard" for cancer pain management. Its appropriate use by effective pain management improves patient's quality of life. Morphine should be prescribed and used based upon the intensity of pain, irrespective of the prognosis or stage.

Myth#7 Morphine causes intractable side-effects.

Fact#7 Morphine is associated with side-effects such as sedation, cognitive impairment, nausea, vomiting and constipation, etc. Majority of the side-effects are self-limiting to which tolerance develops with time.[10] The exception to this is constipation to which tolerance does not develop and hence requires prophylactic use of laxatives. It has rightly been said "A hand which writes morphine should also prescribe a laxative".

Myth#8 There is no need to give other analgesics with morphine.

Fact#8 Morphine is frequently combined with step I analgesics like acetaminophen/NSAIDs and adjuvants as they have been found to have opioid sparing effect. Cancer pain is multi-faceted, therefore, different analgesics are required in varying combination to target different types of pain.

REFERENCES

1. American Cancer Society. 2002. Cancer facts and figures 2002 [online]. Accessed 4 April 2006. URL: http://www.cancer.org/docroot/STT/STT_0.asp.
2. Pharo GH, Zhou L. 2005. Pharmacologic Management of Cancer Pain. JAOA, 105:S21–28.
3. Downing J. Palliative care: pain. Nurs Times. 1997;93(34):9–12.
4. Anita A, Chan LS. Understanding of the concept of ''Total Pain''. Journal of Hospice and Palliative nursing 2008;10(1):26–32.
5. Ripamonti CI, Bandieri E, Roila F. Management of cancer pain: ESMO Clinical Practice Guidelines. Ann Oncol (2011);22(suppl 6):vi69–vi77.
6. Portenoy RK. 1996. Opioid therapy for chronic nonmalignant pain: A review of the critical issues. J Pain Symptom Manage, 11:203–17.
7. Nersesyan H, Slavin KV. Current approach to cancer pain management: Availability and implications of different treatment options. Therapeutics and Clinical Risk Management. 2007; 3(3):381–400.
8. Mercadante S, Gebbia V, David F, Aielli F, Verna L, Casuccio A, et al. Tools for identifying cancer pain of predominantly neuropathic origin and opioid responsiveness in cancer patients. J Pain 2009;10:594–600.
9. Gallagher R. Killing the symptom without killing the patient. Canadian Family Physician. 2010;56(6):544–546.
10. Chapman SL, Byas-Smith MG, Reed BA. Effects of intermediate-and long-term use of opioids on cognition in patients with chronic pain. ClinJ Pain2002;18(Suppl 4):S83–90.

SECTION

VII

Management of Widespread Pain

Rammurthy and Palak Chavda (Section Editors)

32. Widespread Pain
33. Fibromyalgia
34. Painful Diabetic Neuropathy
35. Myths in Widespread Pain

CHAPTER

32

Widespread Pain

Tarun Kumar Reddy

INTRODUCTION

Chronic widespread pain (CWP) in many ways remains a challenge for the medical profession, but most of all, hell for the patients, who are often dismissed as malingerers, may be forced to give up work and become increasingly isolated, misunderstood, and frustrated. They descend into a spiral of low self-esteem, lack of confidence and poor sleep, and lose interest in all the things that made their lives worth living.

Chronic widespread pain (CWP), including fibromyalgia, is a highly prevalent condition with a range of disabling symptoms, both physical and psychological. The prevalence of CWP has been estimated to be between 7% and 13% of the population. Among men, the prevalence of CWP has been found to be between 3% and 9% and among women between 6.5% and 16%[1,2]. However, studies have shown that CWP prevalence has increased markedly especially in women. While there are no clear reasons for this, possible speculation is "GPs are becoming more familiar with it, and patients are becoming more aware of it. One more important reason is that we are more exposed to stress in the modern era. Lifestyles are more hectic, we are never out of contact, never have the chance to relax and chill out. Then there are changes in the structure of the workplace, people are less secure, less satisfied. It is clear that physical and psychological stressors are very important."

Chronic widespread pain was defined as **the presence of pain, as follows, for at least three months: pain on the left side of the body, pain on the right side of the body, pain above the waist, pain below the waist and axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back).**[3] In this definition, left or right shoulder and buttock pain was considered to be pain in each involved side. Low back pain was considered lower segment pain.

Important features associated with CWP are fatigue, sleep disturbances, stiffness, symptoms of depression and anxiety and cognitive difficulties.[4,5] In addition, high comorbidity of CWP with conditions such as chronic fatigue syndrome, headache, depression, and anxiety have been reported.[6,7] CWP not only causes profound individual suffering and disability in activities of daily living but also associated with high health care utilization and increased health care costs.[8]

RISK FACTORS

There are no single risk factors but there are external and internal factors at play.

1. **Genetic predisposition:** Some people may be genetically predisposed to have a different response to stress than others, or

their endogenous pain control mechanisms do not work as well in some people.

2. **Physical factors:** It is becoming clear that **physical de-conditioning** is also important, and this may be either a consequence or a cause of having pain .
3. **Diet factors:** Diet may also play a part. For example, there is a higher incidence of CWP in non-Caucasians who are more prone to be vitamin D-deficient.

CAUSES OF CWP

1. Non-inflammatory causes

a. **Fibromyalgia**: It is explained in detail elsewhere in the book.

b. **Major depression with somatization:** Pain symptoms are present in 65% of depressed patients and anywhere from 5 to 85% of patients with pain suffer from depression. Low energy, insomnia, and hopelessness resulting from depression and anxiety perpetuate and aggravate physical pain, it becomes almost impossible to tell which came first or where one leaves off and the other begins.

Normally, the brain diverts signals of physical discomfort so that we can concentrate on the external world. When this shutoff mechanism is impaired, physical sensations, including pain, are more likely to become the center of attention. Brain pathways that handle the reception of pain signals, including the seat of emotions in the limbic region, use some of the same neurotransmitters involved in the regulation of mood, especially serotonin and norepinephrine. When regulation fails, pain is intensified along with sadness, hopelessness, and anxiety. And chronic pain, like chronic depression, can alter the functioning of the nervous system and perpetuate itself.

c. **Chronic fatigue syndrome:** In chronic fatigue syndrome, the fatigue is overwhelming and lasts for at least 6 months. It may get worse after physical or mental exertion and a full night's sleep provides no relief. The fatigue is often accompanied by chronic recurring pain, including headaches, sore throat, muscle pain, and joint pain. The joint pain is not associated with signs of redness or swelling.

2. Inflammatory causes: Chronic widespread pain can be associated with the following diseases.

a. Inflammatory arthropathies (rheumatoid arthritis)
b. Polymyositis and dermatomyositis
c. Systemic lupus erythematosus
d. Polymyalgia rheumatica
e. Hypothyroidism
f. Sjögren's syndrome

DIAGNOSTIC CRITERIA

1. **Fibromyalgia:** The diagnostic criteria of fibromyalgia according to **ACR 2010** guidelines are discussed elsewhere in the book.
2. **Major depression with somatization:** Major depression can be diagnosed using **DSM-IV criteria**. Psychiatrist referral is needed to confirm depression.
3. **Chronic fatigue syndrome:** It is diagnosed when the patient has
   - Severe fatigue for at least 6 months not explained by other conditions.
   - And at least four of these symptoms:
     - Headaches
     - Memory or concentration trouble
     - Tender neck or under arm lymph nodes
     - Muscle pain
     - Sore throat
     - Multi-joint pain without swelling or redness
     - Unrefreshing sleep
     - Exhaustion after physical or mental activity.

4. **Rheumatoid arthritis (RA):** According to ACR 2010 Guidelines

Criteria for RA (score-based algorithm: add score of categories A–D; score of >6/10 is needed for classification of a patient as having definite RA)	*Score*
a. Joint involvement	
1 large joint.	0
2–10 large joints	1
1–3 small joints (without involvement of large joints)	2
4–10 small joints (without involvement of large joints)	3
>10 joints (at least 1 small joint)	5
b. Serology (at least 1 test result is needed for classification)	
Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3
c. Acute phase reactants (at least 1 test result is needed for classification)	
Normal CRP *and* normal ESR	0
Abnormal CRP *or* abnormal ESR	1
d. Duration of symptoms	
<6 weeks	0
>6 weeks	1

MANAGEMENT OF WIDESPREAD PAIN

Investigations

Simple laboratory testing is important in the evaluation of patients with chronic widespread pain. No laboratory investigation confirms a clinical diagnosis of fibromyalgia and unnecessary investigations should be avoided. Simple blood testing including a complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), creatine kinase, and thyroid stimulating hormone (TSH) should be done to rule out the differential diagnosis.

Common investigations needed for evaluation of chronic widespread pain are discussed below:

1. **Complete blood count:** Hemoglobin, whiteblood cells count, platelet count should be done. Anemia may be due to chronic disease like hypothyroidism. Platelet count may be high in inflammatory arthropathy like rheumatoid arthritis and may be decreased in SLE. Leucopenia is seen in SLE.
2. **Acute phase reactants:** High erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) can be helpful in distinguishing inflammatory from other joint conditions but they are not very sensitive and are very non-specific. ESR 30 mm/hr or greater and C-reactive protein level greater than 0.7 pg/ml are considered significant. A normal ESR does not rule out the presence of inflammatory arthritis.
3. **Auto-antibodies:** Important auto-antibodies needed for evaluation of patients of chronic widespread pain are discussed here.
   a. **Rheumatoid factor:** Rheumatoid factor, which is autoantibody reactive with the Fc portion of IgG, is found in more than two-thirds of adults with rheumatoid arthritis. The presence of rheumatoid factor is not specific for RA, as rheumatoid factor is found in 5% of healthy persons. The presence of rheumatoid factor does not establish the diagnosis of RA, as the predictive value of the presence of rheumatoid factor in determining a diagnosis of RA is poor. However, the presence of rheumatoid factor can be of prognostic significance because patients with high titers tend to have more severe and progressive disease with extra-articular manifestations. In summary, a test for the presence of rheumatoid factor can be employed to confirm a diagnosis in individuals with a suggestive clinical presentation, and if present in high titer to designate patients at risk for severe

systemic disease. Rheumatoid factor may be positive in systemic lupus erythematosus, Sjögren's syndrome, chronic liver disease, sarcoidosis.

b. **Anti-cyclic citrullinated peptide (anti-CCP/ACPA):** An antibody to a substance called cyclic citrullinated peptide (CCP) has been found to be more specific than rheumatoid factor in rheumatoid arthritis and may be more sensitive in erosive disease. It is positive in 80 to 90% of patients.[9]

c. **Anti-nuclear antibodies (ANA):** In SLE diagnostically, the most important autoantibodies to detect are ANA since the test is positive in > 95% of patients, usually at the onset of symptoms. A few patients develop ANA within 1 year of symptom onset; repeated testing may thus be useful. ANA-negative lupus exists but is very rare in adults, and is usually associated with other autoantibodies (anti-Ro, anti-DNA). High-titer IgG antibodies to double-stranded DNA (ds DNA) (but not to single-stranded DNA) are specific for SLE.

4. **Other markers**

a. **HLA B27:** It is mostly positive in ankylosing spondylitis and other spondyloarthropathies. The presence of HLA B27 is neither necessary nor sufficient for the diagnosis. However, in accord with Bayes' theorem, the presence or absence of HLA B27 greatly increases or decreases, respectively, the probability of ankylosing spondylitis in patients with equivocal clinical findings lacking radiographic abnormalities.

b. **Thyroid markers: Thyroid stimulating hormone (TSH), T3, T4** should be ordered if hypothyroidism is suspected.

c. **Creatine kinase (CK):** Levels should be checked if polymyositis (PM) or dermatomyositis (DM) is suspected. The most sensitive enzyme is CK, which in active disease can be elevated as much as 50-fold. Although the CK level usually parallels disease activity, it can be normal in some patients with active DM, especially when associated with a connective tissue disease. The CK is always elevated in patients with active PM.

Treatment

The usual treatment of chronic widespread pain patients from their general practitioners involve a referral to a rheumatologist and possibly being given a low-dose antidepressant commonly prescribed to patients like amitriptyline. We cannot achieve good results only with pharmacological therapies. Non-pharmacological treatment plays a very important in the management.

1. **Non-pharmacological methods:**

a. **Exercise:** The aim of the exercise programme is to gradually increase their activity levels and fitness. They will not be in very good condition to do exercise may be due to arthritis or their condition, such as fear of movement, and that exercise is going to increase their pain. We should try to break that cycle of pain, by being motivational, supportive and reassuring. Motivation is certainly key as it could be difficult to motivate people whose condition makes them tired, in pain, and often unable to concentrate or focus.[10] We should ask them to build up slowly, and improve their exercise and activity tolerance. We should start them with a level they are comfortable with, and increase the duration and intensity, so as to avoid exacerbating their pain. Patients will feel relaxed, improve their sleep patterns and relieve stress if they exercise regularly.

b. **Cognitive behavioural therapy (CBT):** Although CBT is a complex process, in effect it will focus on how pain has an impact on a person's everyday life and activities, and how it affects their thinking and behavior. In simple terms", **It concentrates on what the patient would like to do with their life, and**

how the pain is stopping them from doing that, helping people to move on". There are various techniques within CBT, such as **cognitive re-structuring**, which is a way of changing negative thoughts by looking at them afresh and challenging them, and **behavioural activation**, which focus on re-establishing daily routines in a paced way. Through CBT we are not curing chronic pain but patients can manage chronic pain in a much better way.

c. **Psychotherapy:** Psychotherapy helps demoralized patients and their families tell their stories and describe the experience of pain in its relation to other problems in their lives.

d. Hypnosis, meditation and progressive muscle relaxation also helps in chronic pain patients associated with depression.

1. **Pharmacological treatment:** Pharmacological drugs used in chronic widespread pain are discussed below. Drugs used in fibromyalgia are discussed elsewhere in the book.

A. Antidepressants: The most versatile of all psychiatric drugs, the antidepressants have an analgesic effect that may be at least partly independent of their effect on depression since it seems to occur at a lower dose. Relieving anxiety, fatigue, depression, or insomnia with mood stabilizers, benzodiazepines, or anticonvulsants will also ease any related pain.

a. **Tricyclic antidepressants: Amitriptyline**, a tricyclic, is one of the antidepressants most often recommended as an analgesic, partly because its sedative qualities can be helpful for people in pain.

b. **Selective serotonin reuptake inhibitors (SSRIs)** such as **fluoxetine** and **sertraline** may **not be quite so effective as pain relievers**, but their side effects are usually better tolerated, and they are less harmful or riskier than tricyclic drugs. They are mainly used to treat depression.

c. **Seratonin norepinephrine reuptake inhibitors (SNRIs)** such as **Duloxetine** and **milnacipran** are used as pain relievers. Duloxetine is started with the dose of 20 mg once or twice a day and the dose is increased up to 120 mg. Milnacipran is started with 25 mg twice a day and dose increased up to 100 mg. They play a very good role in chronic musculoskeletal pain and also C-fiber associated pain.

B. Drugs used in rheumatoid arthritis: Disease modifying antirheumatic drugs (DMARDs) and biologicals are used in RA. Treatment should be given according to ACR 2010 guidelines.

a. **DMARDs:** Methotrexate, sulphasalazine and hydroxychloroquine are the drugs commonly used. They can be used as a monotherapy or combination of two drugs depending on the severity. Methotrexate 20 mg is used weekly once. It can be combined with any other DMARDs.

b. **Tumor necrosis factor inhibitors (TNFi) Biologicals:** Adalimumab, certolizumab pegol, etanercept, infliximab are the biologics used in RA. Rheumatologists reference is a must before starting biologicals.

c. **Non-TNFi Biologics:** Abatacept, rituximab, tocilizumab are also used in some cases.

d. Short term **glucocorticoid therapy** can also be used in refractory cases.

C. Referral to the rheumatologist for further treatment is necessary to treat diseases like SLE, polymyositis or dermatomyositis, hypothyroidism, etc.

Conclusion: Chronic widespread pain is often misdiagnosed in many patients. Prompt diagnosis and treatment is of utmost importance. Non-pharmacological modes of treatment and treatment of the underlying coexisting disease (depression, rheumatoid arthritis, etc.) is very important.

REFERENCES

1. Bergman S, Herrstrom P, Hogstrom K, Petersson, IF, Svensson, B, and Jacobsson, LT Chronic musculoskeletal pain, prevalencerates, and sociodemographic associations in a Swedish population study. *J Rheumatol, 2001;28*(6),1369–77.
2. Gerdle B, Bjork J, Coster L, Henriksson K, Henriksson C, and Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. *BMC Musculoskelet Disord, 2008; 9*, 102.
3. Wolfe F, Smythe HA, Yunus MB, et al. The American college of rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33(2):160–72.
4. Mease P, Arnold LM, Choy EH, Clauw DJ, Crofford, LJ, Glass JM, et al. Fibromyalgia syndrome module at OMERACT 9:domain construct. *J Rheumatol, 36*(10), 2318–29.
5. Wolfe, F, Ross, K, Anderson, J, Russell, IJ, and Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum, 1995;38*(1), 19–28.
6. Aaron LA, Buchwald D. Chronic diffuse musculoskeletal pain, fibromyalgia and co-morbid unexplained clinical conditions. Best Pract Res Clin Rheumatol 17:563–74.
7. Bradley LA. Psychiatric comorbidity in fibromyalgia. Curr Pain Headache Rep 2005;9:79–86.
8. White KP, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study: direct health care costs of fibromyalgia syndrome in London, Canada. J Rheumatol 1999;26(4):885–9.
9. Nishimura K, Sugiyama D, Kogata Y, et al. Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. Ann Intern Med 2007 Jun5;146(11):797–808.
10. http://www.arthritisresearchuk.org/arthritis-information/arthritis-today-magazine/142-autumn-2008/chronic-widespread-pain.
11. Jasvinder Singh, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care and Research.

CHAPTER

33

Fibromyalgia

Rammurthy

INTRODUCTION

Fibromyalgia (FM) is the most important cause of widespread pain and is a common medical condition affecting the general population. FM is not a new disease. In 1850, Froriep described hard places in the muscles of patients with 'rheumatism'. Which were painful to pressure. The term 'firomyalgia' was introduced by Hench in 1976.[1] The estimated prevalence ranges from 2% to 12%[2,3] and is common in all ethnic groups. The prevalence increases with age with peak in fifth to seventh decade. It is more common in females. In general population female to male ratio is 3:1.[1] Middle aged females are most commonly affected.[4] The common association of FM with other rheumatic disorders, chronic viral infections, and systemic illnesses has been well documented in several studies. Diseases like inflammatory bowel disease, thyroid diseases are associated with fibromyalgia. Up to 65% of patients with systemic lupus erythematosus meet the criteria for FM.[3] There is a strong familial association with fibromyalgia and the first degree relatives of the patients are more prone to develop fibromyalgia.[3,5] The patients with fibromyalgia display diffuse hyperalgesia and/or allodynia.[5] This suggest that these individuals have a fundamental problem with pain or sensory processing rather than an abnormality confined to the region where the patient is currently experiencing the pain.

Pathophysiology

FM patients display increased neuronal activation in comparison to controls when the same low-intensity stimulus is applied to both the groups. The pathophysiology of the fibromyalgia is not fully understood. One of the key feature of FM pain is increased sensitivity or hyper-responsiveness. Clinically this is menifested as 'allodynia' or hyperalgesia'. Tneder points in FM are menifestation of allodynia.

Patients with fibromyalgia show an elevated level of biomarkers associated with pain especially glutamate and substance P. They also show an elevated levels of endogenous opioids which explain the lack of response to opioid therapy.[4] Similarly the levels of serotonin is low in patients with fibromyalgia.

Genetic polymorphism: Recent studies have suggested that specific genetic polymorphism are associated with the risk of development of fibromyalgia. Serotonin 5HT2A receptor polymorphism T/T phenotype, serotonin transporter, dopamine-4 receptor, COMT polymorphism have been identified as risk factors for developing fibromyalgia. All these polymorphisms involve the metabolism or transport of monoamines which play critical role in human stress response.[4, 5]

Mechanical factors like uncomfortable posture at work, monotonous work[6] are also considered as the risk factors for the development of FM.

Psychological factors like increased physical complaints and illness behavior, low physical activity, sleep disorders, permanent threat to life, physical abuse in childhood and adulthood, sexual abuse in childhood and adulthood, stress at workplace.[6]

Lifestyle factors like smoking and overweight.[6]

Childhood factors hospitalization after traffic accident, institutionalization, maternal death, financial need.[6]

Dysfunction of the hypothalamopituitary adrenal axis, hypothalamopituitary gonadal axis, hypothalamopituitary growth hormone has been noted in the development of fibromyalgia. Severe deficiency of growth hormone has been noted in fibromyalgia patients. Growth hormone production is severely affected due to sleep disturbances. Immune system abnormalities are also noted in fibromyalgia. Serum IL-8, IL-6 levels have been elevated in these patients.[4, 6]

Autonomic nervous system: A number of differences in the function of the autonomic nervous system among patients with FM and healthy subjects have been described (e.g. decreased heart rate variance, a tendency for syncope, altered cutaneous capillary responsiveness).[6]

Associated Disorders[7] (Table 33.1)

Clinical Features of Fibromyalgia

The clinical features of fibromyalgia are more complex and include wide variety of symptoms.

The most common presenting complaint of patients with FM is 'pain all over body'.

Pain: The patients with fibromyalgia will have widespread body pain. The patient should have pain in at least 11 out of 19 areas where the diagnosis can be made.

Stiffness: These patients will also have morning stiffness which can last from 45 min to 4 hours.

Fatigue is another important symptom which is present in about 80% of patients with fibromyalgia. It ranks second after pain as the most disabling symptom by many patients.

Cognitive dysfunction: These patients often have cognitive dysfunction which range from difficulty in reading books to short term memory loss.

Affective disorder: Up to 40% of patients with fibromyalgia have associated mood disorders like depression and anxiety.There is also a high incidence of insomnia, unrefreshening sleep.

Musculoskeletal	*Genitourinary*	*Gastrointestinal*	*Miscellaneous*
• Nondermatomal paresthesia	• Dysmenorrhea	• Irritable bowel syndrome	• Tension/migraine headaches
• Temporomandibular joint syndrome	• Interstitial cystitis	• Esophageal dysmotility	• Mitral valve proplapsed
• Hypermobility syndrome	• Female urethral syndrome		• Allergy
• Restless legs syndrome	• Vulvar vestibulitis		• Vestribular disorders
• Rheumatoid arthritis	• Premenstrual syndrome		• Ocular disturbances
• Systemic lupus erythematosus			• Anxiety disorders
• Sjögren syndrome			• Reynaud phenomenon
• Osteoarthritis			• Thyroid dysfunction
• Chronic fatigue syndrome			• Lyme disease
• Carpal tunnel syndrome			• Hyperventilation
• Myofascial pain syndrome			• Cognitive dysfunction

The 2010 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia.[8]

Criteria

A patient satisfies diagnostic criteria for fibromyalgia if the following 3 conditions are met:

1. Widespread pain index (WPI) ≥ 7 and symptoms severity (SS) scale score ≥ 5 or WPI 3 – 6 and SS scale score ≥ 9
2. Symptoms have been present at a similar level for at least 3 months.
3. The patient does not have a disorder that would otherwise explain the pain.

Ascertainment

1. WPI: note the number areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19.

Shoulder girdle, left	Hip (buttock, trochanter), left	Jaw, left	Upper back
Shoulder girdle, right	Hip (buttock, trochanter), right	Jaw, right	Lower back
Upper arm, left	Upper leg, left	Chest	Neck
Upper arm, right	Upper leg, right	Abdomen	
Lower arm, left	Lower leg, left		
Lower arm, right	Lower leg, right		

2. SS scale score:

   Fatigue

   Waking unrefreshad

   Cognitive symptoms

   For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale

   0 = no problem

   1 = slight or mild problems, gernally mild or intermittent

   2 = moderate, considerable problems, often present and/or at a moderate level

   3 = severe: pervavsive, continuous, life-disturbing problems

   Considering somatic symptoms in general, indicate whether the patient has*

   0 = no symptoms

   1 = a few symptoms

   2 = a moderate number of symptoms

   3 = a great deal of symptoms

The SS scale score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the extent (severity) of somatic symptoms in general. The final score is between 0 and 12.

* Somatic symptoms that might be considered: muscle pain, irritable bowel syndrome, fatigue/tiredness, thinking or remembering problem, muscle weakness, headache, pain/cramps in the abdomen, numbness/tingling, dizziness, insomnia, depression, constipation, pain in the upper abdomen, nausea, nervousness, chest pain blurred vision, fever, diarrhea, dry mouth itching, wheezing, Raynaud's phenomenon, hives/wets, ringing in ears, vomiting, heatburn, oral ulcers, loss of/change in taste, seizures, dry eyes, short ness of breath, loss of appetite, rash, sun sensitivity, hearing difficulties, easy bruising, hair loss, fequent urination, painful urination, and bladder spasms.

Diagnosis of Fibromyalgia

The American College of Rheumatology (ACR) has framed a diagnostic criteria which was revised in 2010 for the diagnosis of fibromyalgia.[8] In the previous criteria, the identification of tender points by palpation was necessary for the diagnosis. But in the recent 2010 criteria, the palpation of tender points has been removed and only identification of the painful areas by questionnaire has been included in the diagnostic criteria.

The 2010 American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia.[8]

Investigations[7]

There are no specific test that is diagnostic of fibromyalgia. Fibromyalgia is a diagnosis of exclusion. The diagnosis should be made after

ruling out all other causes of widespread pain. Hence the investigations that are to be done include:

1. Complete blood count, erythrocyte sedimentation rate, C-reactive protein.
2. Rheumatoid factor, anti-nuclear antibody.
3. Thyroid function testing.
4. Liver and renal function testing.
5. Creatinine phosphokinase.

DIFFERENTIAL DIAGNOSIS[1]

1. Hypothyroidism
2. Myopathies
3. Rheumatoid arthritis
4. Primary generalised osteoarthritis
5. Hypermobility syndrome
6. Connective tissue disease such as SLE, Sjogren's disease.

Management of Fibromyalgia

Fibromyalgia should be recognised as a complex and heterogeneous condition where there is abnormal pain processing and other secondary features. Optimal treatment requires a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities tailored according to pain intensity, function, associated features such as depression, fatigue and sleep disturbance in discussion with the patient.[9]

Non-pharmacological Therapies

1. Patient education is an important component of the management of fibromyalgia. The treating physician should be empathetic, open and honest and should not demonstrate negative attitude. Attention should be paid to individual symptom in a patient tailored approach. Patients and health care professionals should acknowledge that genetic factors as well as previous adverse events may have contributed to the development of FM, but focusing excessively on a triggering event could compromise patient care and should, therefore, be discouraged.[9, 10]
2. Exercise therapy—individuals with FM should participate in a graduated exercise program including aerobic exercise of their choosing to obtain global health benefits and probable effects on FM symptoms. Individuals with FM should be encouraged to pursue as normal a life pattern as possible, using pacing and/or graded incremental activity to maintain or improve function. In fact regular physical activity has shown to prevent chronic pain syndromes.[9, 11]
3. Psychological interventions—psychological evaluation of the patient to address the associated psychological issues like depression, anxiety, sleep disturbances may be helpful. Cognitive behavioural therapy has shown to be useful in these patients.[9,11]
4. Heat therapy in the form of hot baths or shower (moist heat) or dry heat can also be useful for body pain and stiffness. It can help in relaxing the muscles, facilitate exercise and improve sense of well being.[9]

Pharmacological Therapies

The physician must identify the most bothersome symptoms to help direct pharmacological treatment. An ideal combination would be one which addresses multiple symptoms at the same time with minimum side effects and drug interactions.

The drugs which are approved by FDA for the treatment of fibromyalgia include:[4]

1. Pregabaline (first to get approval by FDA)
2. Duloxetine
3. Milnacipran

These drugs also have been recommended by EULAR for the treatment of fibromyalgia with strong evidence (class Ia).

1. Anticonvulsants

Pregabaline is an anti-epileptic drug which acts at the $\alpha 2\delta$ subunits of voltage gated

calcium channels. It reduces the pain and fatigue in fibromyalgia patients. It is started with low dose of 75 mg once or twice daily and gradually increased depending on the tolerance of the patient. Usual side effects are dizziness and somnolence.

Gabapentin is another drug belonging to same category. The starting dose is 100 mg twice or thrice a day and then the dose is increased depending on the response.

2. SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors)

Duloxetine and milnacipran are the SNRIs (serotonin and norepinephrine reuptake inhibitors) which are having a strong evidence with class Ib recommendation for the treatment of fibromyalgia. These drugs treat depression in addition to the pain. Duloxetine is started with the dose of 20 mg once or twice a day and the dose is increased up to 120 mg. Milnacipran is started with 25 mg twice a day and dose increased up to 100 mg.

The most frequent side effect of both duloxetine and milnacipran is nausea. Other common side effects are dry mouth, constipation, decreased appetite, somnolence, increased sweating and agitation.

3. Tricyclic Antidepressants

Amitriptyline given in low doses of 10 mg has shown to improve the symptoms especially the sleep in patients with fibromyalgia. Another drug of the same group is nortriptyline.

4. SSRIs (Selective Serotonin Reuptake Inhibitors)

Drugs like fluoxetine, fluoxamine, sertraline, citalopram fall under the group SSRI, which are used only in case of fibromyalgia as analgesics. These drugs are also strongly recommended (strength A) and level of evidence is Ib.

5. Tramadol

Tramadol can be used in the doses of 50 mg twice a day to up to 100 mg thrice a day. It has a high level of evidence (class Ib) for its use in fibromyalgia.

Other strong opioids are not recommended for the use in the treatment of fibromyalgia.

6. Paracetamol

Simple analgesic like paracetamol has a weak strength of recommendation and low level of evidence IV for the treatment of fibromyalgia. It can be combined with other drugs.

Drugs like NSAIDs and steroids are not recommended for the treatment of fibromyalgia.

Conclusion

Fibromyalgia is a complex disease where the pathophysiology is not fully under stood. Multidisciplinary approach is required to treat the patients with fibromyalgia.

REFERENCES

1. Bijlsma J, Hachulla E. EULAR textbook on rheumatic disease. 3rd Ed. London: BMJ publishing group Ltd, 2018.
2. Goldenberg DL, Burckhardt C, Crofford L. Management of Fibromyalgia Syndrome. JAMA. 2004; 17 (292):2388–95.
3. Neumann L, Buskila D. Epidemiology of Fibromyalgia. Curr Pain Headache Rep. 2003; 7:362–8. (Queiroz LP. Worldwide Epidemiology of Fibromyalgia. Curr Pain Headache Rep. 2003; 17:356.)
4. Benzon HT, Rathmell JP, Wu CL, Turk DC, Argoff CE, Hurley RW. editors. Practical management of pain. 5th ed. Elsevier. Philadelphia.2014.
5. Fishman SM, Ballantyne JC, Rathmell JP. Editors. Bonica's Management of Pain. 4th ed. Lippincott. Williams and Wilkins.Philadelphia. 2010.
6. Sommer. C, Häuser. W, Burgmer. M, Engelhardt. R, Gerhold. K,/Petzke. F, et al.Etiology and pathophysiology of fibromyalgia syndrome.Der Schmerz. June 2012; 7 :1–7.

7. Jahan F, Nanji K, Qidwai W, Qasim R. Fibromyalgia Syndrome: An Overview of Pathophysiology, Diagnosis and Management. Oman Medical Journal. 2012. 27; 3: 192–5.
8. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. Arthritis Care & Research. 2010. 62; 5: 600–10.
9. Carville SF, Arendt-Nielsen S, Bliddal H, Blotman F, Branco JC, Buskilla D, et al. EULAR evidence based recommendations for the management of fibromyalgia syndrome. Ann Rheum Dis. 2007: 1–26.
10. M-A Fitzcharles, PA Ste-Marie, DL Goldenberg, Pereira JX, Abbey S, Choinière M, et al; the National Fibromyalgia Guideline Advisory Panel. 2012 Canadian guidelinesfor the diagnosis and management of fibromyalgia syndrome: Executive summary. Pain Res Manag. 2013; 18(3):119–26.
11. Ablin J, Fitzcharles MA, Buskila D, Shir Y, Sommer C, Häuser W. Treatment of Fibromyalgia Syndrome: Recommendations of Recent Evidence-Based Interdisciplinary Guidelines with Special Emphasis on Complementary and Alternative Therapies. Hindawi Publishing Corporation. 2013:1–7.

CHAPTER

34

Painful Diabetic Neuropathy

Samarjit Dey

INTRODUCTION

Diabetes is one of the most common causes of neuropathy, with up to 50% of people with type 2 diabetes eventually developing some degree of peripheral neuropathy.[1] Among diabetic neuropathic patients within the UK, between 43% and 53% experienced painful symptoms of the lower limbs. Polyneuropathy induced by diabetes mellitus (DM) is one of the most prevalent forms of neuropathy. Diabetic neuropathy is related to the chronicity of diabetes and to the glycemic control. As the duration of diabetes is beyond our control, every effort should be directed toward tight control of the blood sugar level in order to provide any success to control or prevent painful diabetic neuropathy.[2] Polyneuropathy occurs to a lesser degree also with the non-insulin dependent form of DM, and proper monitoring and control of the glucose level is essential for prevention and intervention.[3] Risk factors for neuropathy include elevated blood glucose levels, elevated triglycerides, high body mass index, smoking and hypertension.[4]

Pathophysiology

Pathogenesis of painful symptoms remains unclear. Many mechanisms are thought to be involved in producing the damage to nerves in people with diabetes. In diabetic neuropathy, a number of metabolic and vascular changes interconnect to cause damage to nerve cells in a similar way to that seen in diabetic retinopathy and nephropathy, with the primary underlying factor being hyperglycaemia.[5,6] Changes include increased oxidative stress, a build-up of glycation end-products, increased activity of the polyol pathway, activation of pro-inflammatory mechanisms and ischemia.[5,6] These processes have direct and indirect adverse effects, not only on neurons and Schwann cells, but also on the vascular tissue of the blood vessels that supply the nerves.[5] All types of nerve fibres, e.g. sensory, autonomic, motor, both myelinated and unmyelinated, are adversely affected in people with diabetes.[5]

TYPES OF DIABETIC NEUROPATHY[14]

A. Generalised neuropathies
   1. Sensory neuropathies
   2. Chronic sensorimotor distal polyneuropthies

B. Focal or multifocal neuropathies
   1. Cranial
   2. Truncal
   3. Focal limb
   4. Proximal motor neuropathy (amyotrophy)
   5. Chronic inflammatory demylinating polyneuropathy

Clinical Features

Symptoms of painful diabetic neuropathy include burning pain, pins and needles, shooting pain down the legs, increased touch sensation (hyperaesthesia) and even numbness.

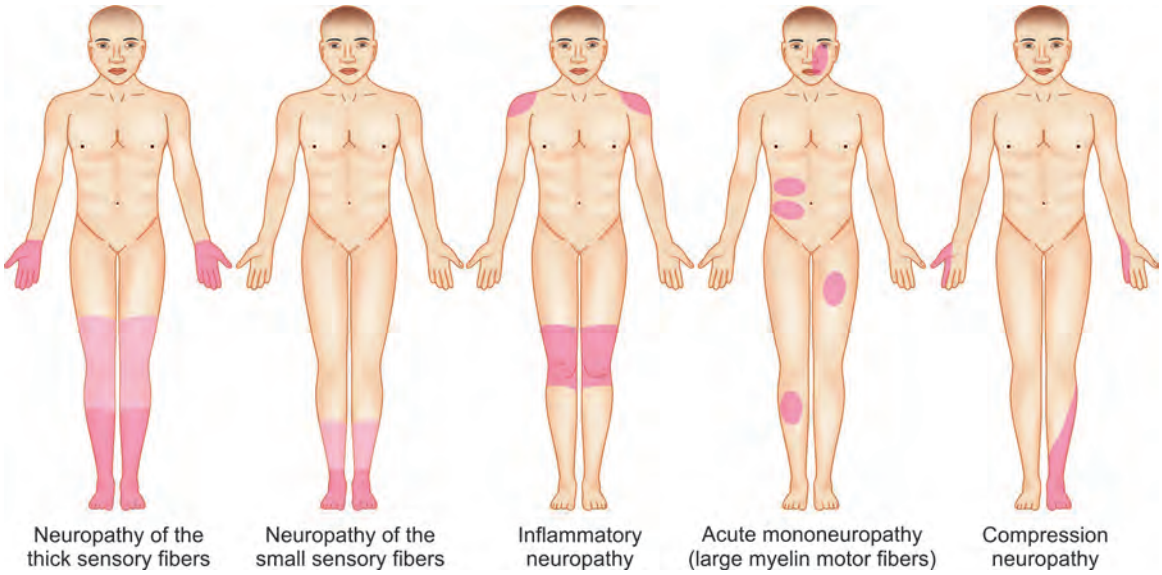

Neuropathy of the thick sensory fibers
Neuropathy of the small sensory fibers
Inflammatory neuropathy
Acute mononeuropathy (large myelin motor fibers)
Compression neuropathy

Fig. 34.1: Types of diabetic neuropathy

The symptoms are distal, symmetrical, often associated with noctturnal exacerbations.

Diagnosis

A. History

More than 80% of the patients with DM-induced poly-neuropathy have a distal, symmetric type of this condition (Fig. 34.1). The symptoms usually present initially in the feet and gradually work their way up.[7]

The initial symptoms are: Signs of diminished sensation; burning feet, which may occur particularly during the night and worsen when touched; and the sensation of tingling in the feet. Attacks of shooting pain also occur.

Examination of a patient with suspected diabetic neuropathy should include:[4]

- A general inspection of the feet and the patient's footwear.
- Musculoskeletal assessment for deformity (including Charcot arthropathy).
- Neurological assessment.
- Vascular assessment of the feet and assessment of the heart rate and blood pressure (lying/sitting and standing).

General inspection of the feet: Examine both feet and check the condition of the skin, particularly looking for erythematous areas, dryness, flakiness, thickness, cracking, callus formation, infection and ulceration.[8]

Musculoskeletal assessment: Callus formation frequently results in a deformity sufficient to cause ulceration. Extreme deformity can develop very acutely in a neuropathic foot, usually in the mid foot and cause a "Charcot foot". Signs of motor involvement may include muscle atrophy, particularly "guttering" between the metatarsals, and muscle weakness beginning with weakness of toe dorsiflexion followed by weakness of foot dorsiflexion.[8,9]

Neurological assessment: The classic pattern of sensory loss in a patient with symmetric distal polyneuropathy is a length dependent, non-dermatomal distal loss affecting all modalities, e.g. light touch, pin prick and temperature.[2] This is referred to as a "sock or stocking" distribution that may extend to the mid-calf.[2] In severe cases it may extend further up the leg and even rarely on to the trunk or involve the upper limbs, beginning in the fingers (a "glove" distribution).[1]

In a patient with diabetes, sensory loss is most often determined with the use of monofilament testing. An ability to detect pain and light touch can be assessed with the use of a sharp examination pin or sterile needle and a wisp of cotton wool. An impairment of the perception of vibration, assessed with a 128 Hz tuning fork, is often regarded as the first objective evidence of symmetric distal polyneuropathy.[4]

The deep tendon reflexes may be reduced or absent, particularly those at the ankle. Some experts regard the loss of ankle reflexes as a cardinal sign of symmetric distal polyneuropathy, however, other possible causes such as an S1 radiculopathy, other focal neuropathies and a tendency for an age-related decrease in the reflexes must also be considered.[2,9]

Vascular assessment: The patient's foot should be palpated to determine the presence and character of the posterior tibial and dorsalis pedis pulses. Further investigation using the ankle-brachial pressure index (ABPI) can provide additional information and help determine the patient's risk of ulceration and the need for referral.[8] On examination, patients who have autonomic neuropathy affecting the cardiovascular system may be found to have a resting tachycardia and orthostatic hypotension, and may report reduced exercise tolerance.

Investigations

Laboratory investigations are not generally required for the diagnosis of diabetic peripheral neuropathy; however, they are usually requested to help exclude other causes of neuropathy. Initial investigations would usually include a full blood count, CRP, HbA_{1c}, liver function tests, creatinine clearance, vitamin B_{12}, folate and thyroid-stimulating hormone tests.[11] **Referral for electrodiagnostic testing** is rarely required, but may be considered for patients with atypical features of neuropathy, e.g. onset of symptoms in the hands, proximal rather than distal weakness or marked sensory ataxia.

Additional Tests[4]

Microscopic examination of nerves with diabetic polyneuropathy showed axonal degeneration and demyelination because of the dysfunction of the Schwann cells. The occurrence of a reduction of the axonal conduction velocity and a conduction delay in the electromyogram (EMG) is helpful to diagnosis. Scoring system for diabetic neuropathy is mentioned in Table 34.1.

Table 34.1: Diabetic neuropathy symptom score (DNS)[11]

DNS items	*Rate*
Unsteadiness in walking	0 = absent, 1 = present
Numbness	0 = absent, 1 = present
Burning, aching pain or tenderness in legs or feet	0 = absent, 1 = present
Prickling sensations	0 = absent, 1 = present

The maximum score of DNS is four points, one point or more indicates neurological abnormalities.

Management (Table 34.2)

1. Intensive glycemic control is the main stay of prevention and treatment.
2. Medications[12]
   The following agents may be used alone or in combination for relief of painful peripheral neuropathy:
   a. Anticonvulsants (pregabalin [Grade A, Level 1], gabapentin, valproate [Grade B, Level 2].
   b. Antidepressants (amitriptyline, duloxetine, venlafaxine) [Grade B, Level 2].
   c. Opioid analgesics (tapentadol ER, oxycodone ER, tramadol) [Grade B, Level 2].
   d. Topical nitrate spray [Grade B, Level 2].

Interventions

Neurostimulation can be considered if an adequate pharmacological treatment does not

Table 34.2: Medications used in diabetic neuropathy[12]

	Suggested starting dose	*Suggested titration if tolerated*	*Suggested maximal tolerate dose*
Anticonvulsants †			
Gabapentin (23, 55)	300 mg bid up to 600 mg po qid	May titrate slowly	3,600 mg/day
Pregabalin (24–26, 30)	75 mg bid	May titrate slowly up to 300 mg po bid	600 mg/day
Valproate (31, 32)	250 mg bid	May titrate slowly up to 500 mg po bid	1500 mg/day
Antidepressants			
Amitriptyline (31, 32)	10 mg qhs	May titrate slowly up to 100 mg po qhs	150 mg/day
Duloxetine (35, 40)	30 mg OD	May titrate to 60 mg po od	120 mg/day
Venlafaxine (37)	37.5 mg bid	May titrate slowly up to 150 mg po bid	300 mg/day
Opioids			
Dextromethorphan (41)	100 mg qid	May titrate slowly up to 200 mg po qid	960 mg/day
Morphine sustained release (55)	15 mg bid	May titrate slowly up to 60 mg po bid	180 mg/day
Oxycodone ER (43)	10 mg bid	May titrate slowly up to 40 mg po bid	160 mg/day
Tapentadol ER	100 mg bid	May titrate slowly up to 250 mg po bid	500 mg/day
Tramadol (44)	50 mg qid	May titrate slowly up to 50 mg po bid	400 mg/day
Others			
Topical nitrate sprays (46, 47, 51)	30 mg spray to legs qhs	May titrate slowly up to 30 mg spray to legs bid	60 mg day
Capsaicin cream (48, 49)	0.075% cream applied 3–4 times per day	May titrate 5–6 times per day	5–6 applications per day

lead to sufficient pain reduction or it is accompanied by serious adverse effects. Role of transcutaneous electrical nerve stimulation is not well established. Spinal cord stimulation (Grade 2 C+) has been proven beneficial.[13]

REFERENCES

1. Tesfaye S, Boulton AJ, Dickenson A. Mechanisms and management of diabetic painful distal symmetrical polyneuropathy. Diabetes Care 2013;36:2456–65.
2. Said G. Diabetic neuropathy—a review. Nat Clin Pract Neurol. 2007;3:331–40.
3. Partanen J, Niskanen L, Lehtinen J, et al. Natural history of peripheral neuropathy in patients with

non-insulin-dependent diabetes mellitus.N Engl J Med.1995;333:89–94.

4. Vinik A, Nevoret M, Casellini C, et al. Diabetic Neuropathy. Endocrinol Metab Clin N Am 2013;42:747–87.
5. Sytze van Dam P. Pathogenesis of diabetic neuropathy: focus on neurovascular mechanisms. Eur J Pharmacol 2013;2013:180–6.
6. Tesfaye S, Boulton A, Dyck P, et al. Diabetic neuropathies: Update on definitions, diagnosis criteria, estimation of severity, and treatment. Diabetes Care 2010;33:2285–93.
7. Franse LV, Valk GD, Dekker JH, et al. "Numbness of the feet" is a poor indicator for polyneuropathy in type 2 diabetic patients. Diabet Med. 2000; 17: 105–110.
8. Boulton A, Armstrong D, Albert S, et al. Comprehensive foot examination and risk assessment. Diabetes Care 2008;31:1679–85.
9. England J, Gronseth G, Franklin G, et al. Distal symmetric polyneuropathy: A definition for clinical research. Neurology 2005;64:199–207.
10. Azhary H, Farooq M, Bhanushali M, et al. Peripheral neuropathy: Differential diagnosis and management. Am Fam Physician 2010;81:887–92.
11. Meijer JW, Smit AJ, Sonderen EV, Groothoff JW, Eisma WH, Links TP. Symptom scoring systems to diagnose distal polyneuropathy in diabetes: the Diabetic Neuropathy Symptom score. Diabet Med. 2002 Nov;19(11):962–5.
12. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes 2013;37(suppl 1):S1-S212.
13. Wouter Pluijms ,Frank Huygen ,Jianguo Cheng ,Nagy Mekhail ,Maarten van Kleef ,Jan Van Zundert,Robert van Dongen. Painful Diabetic Polyneuropathy. Pain Practice. 2011 Mar/ Apr; 11(2): 191–198.
14. Benzon HT,Rathmell JP, Wu CL, Turk DC, Argoff CE, Hurley RW, editors. Practical management of pain. 5th ed. Elsevier. 2014.

CHAPTER

35

Myths in Widespread Pain

Rammurthy

1. **Myth: Widespread pain is due to psychological problem (it is all in the patient's head).**

   Fact: Many physicians think that widespread pain especially fibromyalgia is not a real disease but a form of psychological disorder. It has been proved that fibromyalgia is a distinct disorder. It has been shown in many studies that there is increased levels of biomarkers like substance P, glutamate in these patients. Certain genetic polymorphism is also associated with development of fibromyalgia. Moreover, fibromyalgia has a strong familial component, i.e. it runs in families. A large number of disorders can cause widespread pain and fibromyalgia is an important cause.[1]

2. **Myth: Fibromyalgia and arthritis are same.**

   Fact: Fibromyalgia and arthritis are totally different entities. Arthritis indicates inflammation of the joints. Although rheumatoid arthritis and spondyloarthropathy are the causes of widespread pain, they differ from fibromyalgia in various aspects. Fibromyalgia is a diagnosis of exclusion. The pain in fibromyalgia is neuropathic in nature. The pain is mostly present near the end of the muscle, near myotendinous junction close to the joint, which can be easily mistaken for arthritis. Inflammatory markers are negative in case of fibromyalgia.

3. **Fibromyalgia affects muscles, joints and connective tissues.**

   Fact: For many years it was thought that fibromyalgia is a musculoskeletal disorder. But now it has been proved that fibromyalgia is a disease of the central nervous system, there is no evidence of damage to the joints and muscles. There is a problem in pain processing in these patients and hence they display an increased neuronal activation compared to the controls for a low intensity stimulus.[2]

4. **Myth: Fibromyalgia is a waste basket diagnosis, physician use this diagnosis when he cannot find the cause.**

   Fact: There is a specific set of diagnostic criteria developed by the American College of Rheumatology to be used for diagnosing fibromyalgia. This diagnostic criteria has been revised in 2010.[3]

5. **Myth: There is no definitive treatment for fibromyalgia and hence nothing much can be done.**

   Fact: The fact is although fibromyalgia is a diagnosis of exclusion, there are numerous treatment modalities which are having good evidence and are strongly recom-

mended in the treatment of fibromyalgia. Successful treatment of fibromyalgia depends on multidisciplinary approach patient education, aerobic exercises, cognitive behavioral therapy and proper use of pharmacotherapy. Drugs like SNRIs, pregabalin, gabapentin, TCA are the first line drugs which have high quality evidence in the treatment of fibromyalgia.[4]

REFERENCES

1. Benzon HT, Rathmell JP, Wu CL, Turk DC, Argoff CE, Hurley RW (editors). Practical management of pain. 5th ed. Elsevier. Philadelphia, 2014.
2. Fishman SM, Ballantyne JC, Rathmell JP. (Editors) Bonica's Management of Pain. 4th ed. Lippincott. Williams and Wilkins. Philadelphia, 2010.
3. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. Arthritis Care and Research. 2010. 62; 5: 600–10.
4. Carville SF, Arendt-Nielsen S, Bliddal H, Blotman F, Branco JC, Buskilla D, et al. EULAR evidence based recommendations for the management of fibromyalgia syndrome. Ann Rheum Dis. 2007: 1–26.

SECTION

VIII

Management of Neuropathic Pain

Praneet Singh (Section Editor)

36. Complex Regional Pain Syndrome
37. Acute Herpes Zoster and Postherpetic Neuralgia
38. Phantom Limb Pain
39. Trigeminal Neuralgia
40. Myths in Neuropathic Pain

CHAPTER

36

Complex Regional Pain Syndrome

Abhisesh Shrestha and Shirish Amatya

INTRODUCTION

Complex regional pain syndrome (CRPS) is an inflammatory and neuropathic disorder characterized by involvement of autonomic nervous system. It was described first in 1864 by Silas Weir Mitchell who made an important observation of Civil War soldiers when he noticed that they suffered from burning pain and muscle atrophy at the sites of their injuries. He called this "causalgia," which is derived from the Greek words kausis (burning) and algos (pain).[1]

A review of the literature reveals multiple different names for this syndrome, like Sudeck's atrophy, algodystrophy, post-traumatic dystrophy, and the most frequently used term, reflex sympathetic dystrophy. The term CRPS was coined in 1994 by International Association for the Study of Pain (IASP) in Orlando. IASP defines CRPS as a collection of locally appearing painful conditions following a trauma, which chiefly occur distally and exceed in intensity and duration the expected clinical course of the original trauma, often resulting in considerably restricted motor function.

CRPS is divided into type I and II (also known as reflex sympathetic dystrophy and causalgia respectively). In the course of the disease patient may show varying level of sympathetic nervous system involvement, so defined as sympathetically mediated pain (SMP) or sympathetically independent pain (SIP).

Epidemiology

The real incidence of CRPS is unknown, the incidence per person/year at risk of the disease is 5.46–26.6/100,000. It occurs more commonly in female than male, ratio being 2:3 to 3:1 and increasing with age. Mean age at diagnosis varies between 47 and 52 years.

Pathophysiology

CRPS Type I and Type II differ from each other by the presence (Type II) or absence (Type I) of evidence of nerve injury. Hallmark of the condition includes pain which is manifested spontaneously together with hyperalgesia and allodynia. Associated signs are vasomotor, sudomotor disturbances, passive movement disorders with trophic changes.

The mechanisms involved are multiple.

Altered Cutaneous Innervation Following Injury

There are assumptions that some degree of nerve injury is required however trivial to initiate the cascade of events associated with CRPS.

Peripheral sensitization

Peripheral sensitization resulting from the persistent nociceptive afferent activity as a result of the initial tissue trauma has one of the major role to play in pathophysiology of CRPS. After local tissue injury, the primary afferent fibers in the traumatized area release neuropeptides such as bradykinin and

substance P, which results in increased firing of nociceptors to noxious stimuli and reduced firing threshold to mechanical and thermal stimuli, this may be the cause for hyperalgesia and allodynia.

Central sensitization

Persistence of peripheral sensitization together with release of excitatory neurotransmitter, glutamate, acting at the spinal N-methyl-D-aspartic acid receptors leads to enhanced response of non-noxious and noxious stimuli. They also demonstrate significant wind up phenomenon. This leads to persistence of symptoms associated with central sensitization.

Sympathetically mediated pain

It has been indicated that there is an interaction between the sympathetic noradrenergic neurons in the periphery and the primary afferent neurons as part of the underlying mechanism of sympathetically mediated pain (SMP) in patients with CRPS I. There also has been some suggestions that sympathetic nervous system innervation of deep somatic tissue may be as important as cutaneous innervations as a determinant of the symatho-afferent coupling that occurs particularly in the acute phase of CRPS. They can also occur in mechano, and thermoreceptor.

Inflammatory mediators

Release of proinflammatory cytokines (interleukin IL-2, IL-6, and TNF-α) from mast cell and lymphocytes following tissue injury and secondary release of neuropeptides (substance P, CGRP) following neural inflammation can lead to increased tissue permeability and vasodilatation causing 'warm CRPS' with edema.

Cortical reorganization

It occurs in central somatosensory and motor networks that may result in altered central processing of tactile and nociceptive stimuli and cerebral organization of movement.

Stages of CRPS: Sequential stages of CRPS include

1. **Stage 1:** Early acute stage of CRPS, characterized by pain, sensory abnormalities (hyperalgesia, allodynia), vasomotor, sudomotor dysfunction or prominent edema (Fig. 36.1).
2. **Stage 2:** Dystrophic stage: 3–6 months after onset of disease, more marked pain, sensory dysfunction, continued evidence of vasomotor dysfunction and development of significant motor and trophic changes. Skin turning cold and purple, then warm and flushed.
3. **Stage 3:** Atrophic stage: Decreased pain, sensory disturbance, continued vasomotor disturbance and markedly increased motor/trophic changes. Permanent changes such as muscle atrophy/disabilities develop.

Fig. 36.1: Early acute stage of CPRS

Clinical Diagnosis

The big problem with CRPS is that since the pathophysiology and mechanism is poorly understood, we can only label CRPS as variety of sign and symptoms and exclusion of other possible causes. CRPS is usually preceded by trauma or surgery, the affected area usually extends beyond the original injury.

IASP diagnostic criteria:

1. Presence of an inciting noxious event or a cause of immobilization.
2. Continuing pain, allodynia or hyperalgesia with which the pain is disproportionate to any inciting event.
3. Evidence at some point of edema, changes in skin blood flow or abnormal sudomotor activity in the region of pain.
4. The diagnosis is excluded by the existence of conditions that would otherwise account for degree of pain and dysfunction.

IASP criteria are adequately sensitive, however lacks specificity because vasomotor, sudomotor and edema related changes are taken into same diagnostic criteria instead of considering as distinct elements of the syndrome. Additionally, it failed to include motor/trophic signs and symptoms.

The Budapest criteria[2,3] was devised and formulated in 2003 to overcome the shortcomings of previous diagnostic criteria.

In this together with Type I and II a new category was added: CRPS-NOS (not otherwise specified) which included those patients who did not fulfil the Budapest criteria but whose signs and symptoms could not be better explained by any other diagnosis.

To make the clinical diagnosis, the following criteria must be met:

- Continuing pain, which is disproportionate to any inciting event.
- Must report at least one symptom in all four of the following categories:
  - Sensory—reports of hyperesthesia and/or allodynia.
  - Vasomotor—reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry.
  - Sudomotor/edema—reports of edema and/or sweating changes and/or sweating asymmetry.
  - Motor/trophic—reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
- Must display at least one sign at time of evaluation in two or more of the following categories:
  - Sensory—evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement).
  - Vasomotor—evidence of temperature asymmetry (>1°C) and/or skin colour changes and/or asymmetry.
  - Sudomotor/edema—evidence of edema and/or sweating changes and/or sweating asymmetry.
  - Motor/trophic—evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin).
- There is no other diagnosis that better explains the signs and symptoms.

High sensitivity/low specificity occurs when diagnosis requires at least one each of at least two of the sign categories, and at least one each of two of the symptom categories (0.94 and 0.36, respectively).

While diagnosis of CRPS is primarily based on clinical signs and symptoms, laboratory, neurophysiological, and radiologic testing may be helpful to support or refute a potential determination (Table 36.1). The role of laboratory testing and radiology may be primarily to exclude other diagnostic possibilities.

Treatment

The treatment should center on multimodal pharmacological therapy with effective pain control, functional restoration and enhancement of psychological well-being.

Pharmacotherapy

Nonsteroidal anti-inflammatory drugs (NSAIDs):

There are not a lot of studies proving effectiveness of NSAIDs but in clinical practice it provides mild to moderate pain relief.

Table 36.1: Differential diagnosis of complex regional pain syndrome	
Neuropathic pain syndromes	Peripheral (poly) neuropathy: Nerve entrapment, radiculopathy, postherpetic neuralgia, deafferentation pain after CVA, plexopathy, motor neuron disease
Vascular diseases	Thrombosis: Acrocyanosis, atherosclerosis, Raynaud's disease, erythromelalgia
Inflammation	Erysipelas: Inflammation NOS, bursitis, seronegative arthritis, rheumatologic diseases
Myofascial pain	Overuse: Disuse, tennis elbow, repetitive strain injury, fibromyalgia
Psychiatric problems	Somatoform pain disorders, Munchausen syndrome

Antidepressants

Antidepressant has been the main stay of treatment for neuropathic pain. Norepinephrine and serotonin blockers and selective norepinephrine blockers like amitriptyline (10–75 mg/day) and desipramine (10–75 mg/day), respectively, may exerts their influence by modulating the noradrenergic and serotonergic descending pathway. Moreover the selective serotonin reuptake inhibitor have not shown to be effective than above-mentioned drugs. The added value that these drugs provide is mood elevation and sedation with better sleep pattern. Using tricyclic antidepressant, like amitriptyline in patient above the age of 65 can have potential cardiac side effect.

Anticonvulsant

Gabapentin (900–3600 mg/day) and pregabalin (150–600 mg/day) has shown to be effective in diabetic neuropathy and postherpetic neuralgia. The analgesic effect of gabapentin in CRPS is well-proved by studies.[3] FDA has approved carbamazepine for trigeminal neuralgia and can be considered as second line for CRPS. Its analog, oxycarbamazepine, has no side effect on liver and bone marrow toxicity and can be used as an alternative.

Opioids

Regularly used drugs in this category are morphine 15–60 mg (extended release) or oxycodone 10–60 mg. The common side effects are nausea, vomiting, constipation, sedation. These drugs should be used in multimodal therapy because alone the efficacy of drug is vastly reduced.

Other novel techniques

Free radical scavengers has been tried in form of dimethyl sulfoxide (DSMO) and oral N-acetylcysteine (NAC). Result with vitamin C has also been positive. Bisphosphonates has been shown to decrease pain and swelling in patient with CRPS. Even NMDA receptor antagonist has been tried via different route with variable results (Fig. 36.2).

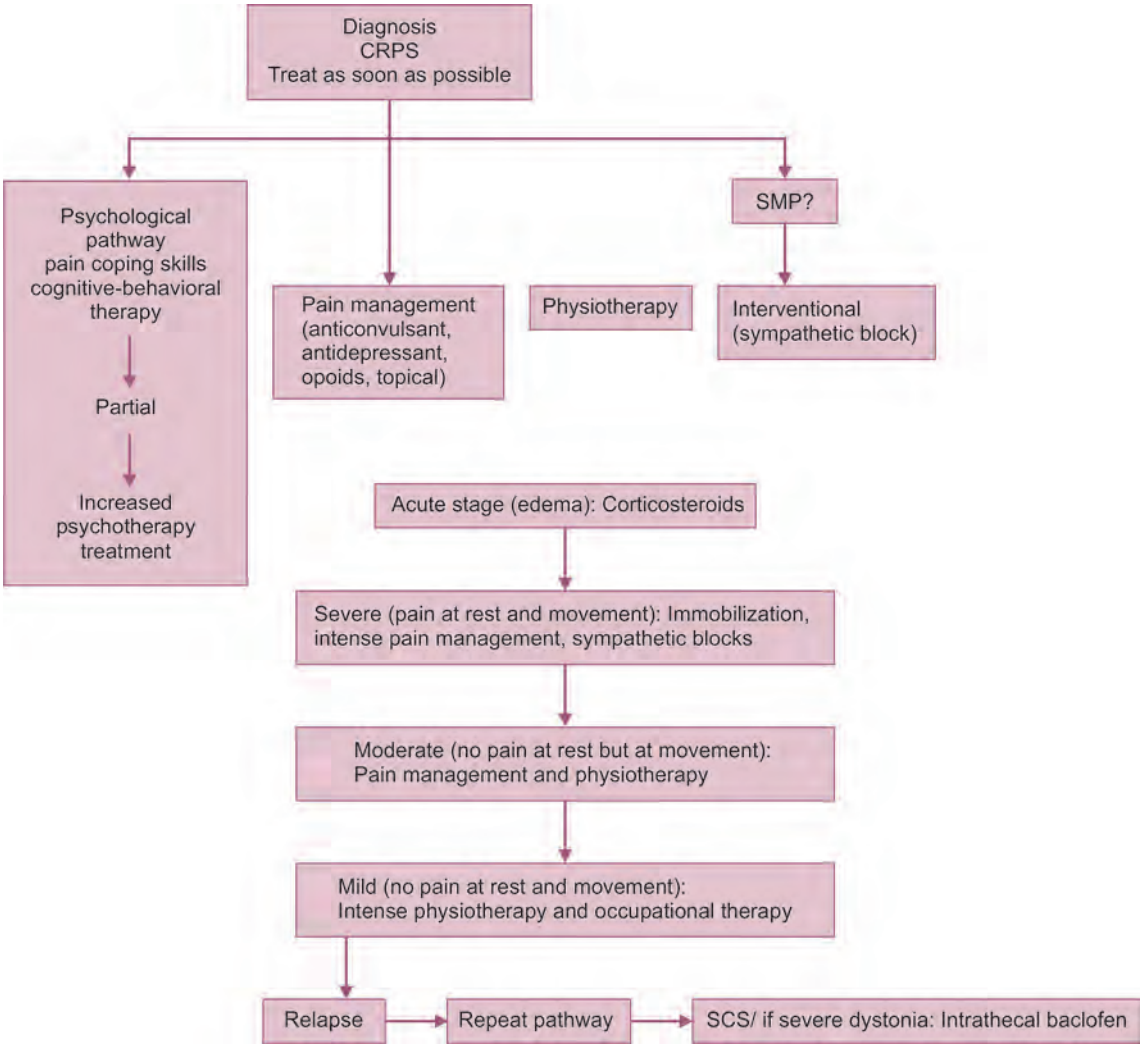
Interventional Therapies

Intravenous Regional Anesthesia

A lot of agents such as guanethidine, droperidol, atropine and lidocaine-methylprednisolone has been tried but strong evidence to such agents have not been proven.

Sympathetic Nerve Blocks

These blocks can be utilized as diagnostic and therapeutic tool. As a diagnostic tool it can differentiate between if the neuropathic pain is sympathetically mediated (SNP) or sympathetically independent (SIP). Sympatholysis is associated with prolonged pain relief in patients who respond to diagnostic test. The analgesia post procedure will allow for further implementation of physical therapy and modalities like desensatization which will ultimately help for better functional restoration of the affected limb.


Diagnosis
CRPS
Treat as soon as possible
Psychological pathway
pain coping skills
cognitive-behavioral therapy
Partial
Increased psychotherapy treatment
Pain management (anticonvulsant, antidepressant, opoids, topical)
Physiotherapy
SMP?
Interventional (sympathetic block)
Acute stage (edema): Corticosteroids
Severe (pain at rest and movement): Immobilization, intense pain management, sympathetic blocks
Moderate (no pain at rest but at movement): Pain management and physiotherapy
Mild (no pain at rest and movement): Intense physiotherapy and occupational therapy
Relapse
Repeat pathway
SCS/ if severe dystonia: Intrathecal baclofen

Intrathecal Baclofen

CRPS can lead to refractory dystonia in many patients, and baclofen (GABA B receptor agonist) that inhibits sensory input into the spinal cord has been shown to effective in many patients.

Spinal Cord Stimulation

There are a lot of study showing effectiveness of SCS in long-term treatment of CRPS. In long-term it is also taken as a cost-effective treatment. For CRPS I the level of evidence is A and for type II it is D.

Fuctional Restoration

This remains the hallmark for the treatment of CRPS. The modality remains on early desensitization and physical therapist addressing muscle strength, flexibility, gait training.

Psychotherapy

Depression and anxiety are common component of CRPS because of uncertainty in cause, course and treatment options. Cognitive-behavioral therapy is found to be the most effective long-lasting psychological intervention.

REFERENCES

1. Schwartzman RJ, Erwin KL, Alexander GM. The natural history of complex regional pain syndrome. The Clinical Journal of Pain. 2009; 25 (4): 273–80.
2. Pergolizzi JV, LeQuang JA, Nalamachu S, et al. The Budapest criteria for complex regional pain syndrome: The diagnostic challenge. Anaesthesiol Clin Sci Res. 2018; 2(1):1–10.
3. Harden N, Bruebl S, Stanton-Hicks M, et al. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med 2007; 8: 326–31.

CHAPTER

37

Acute Herpes Zoster and Postherpetic Neuralgia

Jeshnu Prakash Tople and Pranav Patel

INTRODUCTION

Varicella zoster, a DNA virus causes chickenpox when exposed for the first time. This varicella zoster virus becomes dormant, but can lead to herpes zoster in susceptible individuals after latency of months or years. The virus becomes dormant and remains in sensory ganglia before reactivation. Herpes zoster (HZ) is an acute painful condition associated with rash. This condition in long-term can cause a neuropathic pain syndrome namely post- herpetic neuralgia, the most common complication of herpes zoster.

Risk Factors[1, 2, 3]

- Old age
- Chronic corticosteroid use
- HIV infection
- Cancer
- Make female gender as separate point
- Chemotherapy
- Female gender
- Immunosuppressive therapy
- Greater acute pain severity
- Greater severity of rash during acute phase
- White individuals
- Family history
- Autoimmune diseases like RA, SLE
- Physical trauma
- Comorbidities like asthma, DM, COPD.

Clinical Features[1,2,4]

- Prodrome-usually for 3–7 days before appearance of rash, but can be prolonged.
  - Fatigue
  - Headache
  - Flu like symptoms
  - Hyperesthesia
  - Tingling
  - Pruritis
  - Unilateral dermatomal burning pain
  - Zoster sine herpete—prodromal symptoms without development of characteristic rash.
- Rash
  - Initially maculopapular → vesicular with erythematous bases → pustular rash in next 7–10 days → open lesion with superficial crusting → in 2–3 weeks scabs get cleared → normal skin or hypo or hyperpigmented scarring.
  - Unilateral mostly.
  - Involve one or two contiguous dermatomes.

Most commonly affected dermatomes (with decreasing frequency)—thoracic dermatomes (common—T5 and T6), ophthalmic division of trigeminal nerve, other cranial nerves, cervical, lumbar and sacral dermatomes, rarely diffuse cutaneous or visceral involvement occur.

- Pain
  - Burning/throbbing/stabbing/electric shock like/combination of these.
  - Allodynia and increased tactile sensitivity.

- Worsened with secondary vesicular infection and ulceration as well as muscle spasm.
- May be accompanied by paresthesia/dysesthesia/itching.
- Usually resolves with rash.
- Usually six months after exposure it decreases or resolves, but may be there for years in some patients.
- When persists after the rash, it is called as acute herpetic neuralgia (pain within 30 days of onset of rash), subacute herpetic neuralgia (pain for more than 30 days) or postherpetic neuralgia (pain for 120 or more days).

Pathophysiology[1,2]

Acute varicella infection → chickenpox → latent virus in sensory ganglion (virus remains inactive due to cell mediated immunity) → reativation of virus when cell-mediated immunity gets reduced → replication and transport of newly synthesized virus to axons of the involved sensory ganglion (spinal or cranial) in both the direction central and distal → inflammation and injury to neural tissue in affected dermatome → infectious hemorrhagic necrosis, loss of neural tissue, scarring and fibrosis of sensory ganglion, atrophy of the dorsal horn and decrease in myelinated axons and increase in small unmyelinated axons of the corresponding nerve/s → clinical findings (rash/pain) of HZ along the dermatome of affected sensory ganglion.

Also, anterior horn cells, autonomic neurons, leptomeninges may get involved → muscle weakness, palsy and/or pleocytosis of spinal fluid.

Mechanism of Pain

1. Sensitization—injury to the nerve/s → sensitization of central as well as peripheral receptors → decreased threshold to generate action potential → hyperexcitability and allodynia.
2. Deafferentation—destruction of neural tissue after reactivation of virus → neural tissue regeneration to attempt reconnection of the fibers → hyperalgesia and allodyia.
3. Sympathetic nervous system—inflammation → vasoconstriction → reduced intraneural blood flow, hypoxia, endoneural edema → pain.

Differential Diagnosis[1,5]

- Contact dermatitis
- Herpes simplex virus infection
- Lymphangioma circumscriptum.

Diagnosis[1]

- Clinically mostly
- Viral culture—low sensitivity and high specificity
- Direct immunofluorescence assay—90% sensitivity
- Viral DNA testing by polymerase chain reaction—almost 100% sensitivity and specificity, but expensive
- Biopsy—reserved for difficult to diagnose cases
- Investigate for other underlying diseases if warranted clinically.

Treatment goal[1,4]

- Treatment of rash and acute viral infection
- Treatment of acute pain associated with herpes zoster
- Prevention of central sensitization
- Prevention of postherpetic neuralgia.

Treatment[1,2,4]

- Oral antiviral therapy should be started as soon as possible, ideally within 72 hours of rash appearance
  - *First line of drugs*—acyclovir (800 mg 5 times a day × 7–10 days), famciclovir (500 mg TDS × 7 days), valacyclovir (1000 mg TDS × 7 day)
  - *Second line of drugs*—vidarabine, foscarnet, cidofovir.

Recommended for:	*Benefits include:*
– Elderly patients – Moderate to severe rash – Ophthalmic involvement – Immunocompromised states	– Inhibition of viral replication – Reduces duration of viral shedding – Hastens rash healing – Decrease in degree of neural damage – Decreases severity and duration of acute pain – Decreases duration of postherpetic neuralgia – Decreases incidence of postherpetic neuralgia

- **For pain:**
  WHO ladder for acute pain of HZ
  - Mild pain-NSAIDs/acetaminophen ± mild opioid like tramadol
  - Moderate pain-opioids
  - If above analgesics cannot control pain, adjuvants that can be used include-gabapentin, pregabalin, nortryptyline, desipramine, duloxetine, venlafaxine

Intervention (relieves pain but does not have any effect on prevention of postherpetic neuralgia):
- Continuous/repeated segmental epidural block
- Continuous/repeated intercostal nerve block
- Stellate ganglion block
- Perilesional infiltration of local anesthetic + steroid
- Spinal canal stimulator also have positive outcome

Others
- Open lesions—lotions containing calamine
- Crusted lesion—capsacin cream
- Topical lignocaine

- **Patient education**
  - To avoid contact with seronegative varicella zoster virus individuals or immuno-compromised individuals
  - To maintain nutrition, social and physical activities
  - To avoid skin irritation and secondary infection by keeping the rash area clean, avoiding adhesive dressing or ointment application
  - To be cautious about fever, confusion or other significant constitutional symptoms and to inform physician if it develops

- Corticosteroid—decrease the intensity but not duration of HZ disease nor it prevent development of postherpetic neuralgia. Role is controversial. Prednisolone (30 mg BD × 7 days, then 15 mg BD × next 7 days, 7.5 mg BD × next 7 days).

Complications[1,6]

More in elderly and immunocompromised patients:

- Postherpetic neuralgia—most common.
- Ophthalmic complications—retinitis, keratitis, scleritis, iritis, secondary glaucoma, ptosis leading to impaired vision or complete blindness, delayed contralateral hemiparesis.
- Motor neuropathy—extraocular nerves, fascial nerves, phrenic nerves, intercostals nerves, cervical motor nerve roots and lumbosacral nerve roots, Ramsay Hunt syndrome, Bell's palsy.
- Other—bacterial cellulitis, aseptic meningitis, myelitis, encephalitis, pneumonitis, cerebellar ataxia, encephalitis, Guillain-Barré syndrome, organ dysfunction due to scarring, impaired quality of life.

Prevention[1,7,8]

- Temporary passive immunization-varicella zoster immunoglobulin—to prevent or modify clinical illness in immunocompromised seronegative persons with recent exposure to patients with chickenpox or zoster. Should be administered ASAP once exposed but effective even after 96 hours of exposure.
- Adult vaccine (live, attenuated)—to boost the immunity against herpes zoster. Indicated for individuals 60 years and older, with or without prior episode of herpes zoster. Contraindication—children, pregnant women, and immunocompromised individuals. Side effects—minor, including local skin irritation. Efficacy 5 years.
- Adult vaccine (recombinant zoster vaccine)- indicated for age 50 or more.
- Varicella vaccine to prevent chickenpox-1st dose at age of 15 month onwards and 2nd dose anytime 3 months after the first dose according to IAP 2016 immunization schedule.

POSTHERPETIC NEURALGIA

Postherpetic neuralgia (PHN) is the most common complication of herpes zoster in the immunocompromised patients. This condition results in significant patient suffering and causes a large economic burden to society. The term PHN is defined as dermatomal pain that persists for more than 120 days after the onset of the herpes zoster rash.[9] Pain persisting for more than 180 days after the rash onset is less likely to resolve and hence can be considered "well-established PHN".[10]

Risk Factors for PHN[1]

Common

- Older age
- Severity of rash
- Severity of acute pain
- Prodromal pain

Less common

- Female gender
- Polyneuropathy
- Psychosocial variables
- Ophthalmic distribution

Clinical Features[1,2]

- Stimulus independent pain like intermittent sharp, shooting, or electric shock-like pain and continuous burning or throbbing pain
- Tactile allodynia
- Hyperalgesia
- Sensory abnormalities such as hypoesthetia, alterations in temperature sensation, paresthesias and dysesthesias
- Chronic pruritis
- Areas of hyperpigmentation, hypopigmentation, or scarring in the affected dermatomes following rash healing; a

persistent reddish or brownish hue in affected areas.

- Other—fatigue, insomnia, anxiety, depression and suicidal ideation.

Diagnosis[1,2]

- Primarily based on clinical findings
- Quantitative sensory testing (QST)
- Skin biopsy
- Nerve conduction studies
- Serial serologic assessments.

PATHOPHYSIOLOGY OF PHN[11–14]

- Knowledge of the pathophysiological mechanisms of PHN is quite limited.
- Viral replication is thought to result in a combination of neural and inflammatory damage, leading to peripheral sensitization and central sensitization.
- Deafferentation may also be playing a significant role in the maintenance of PHN.

TREATMENT OF PHN

Pharmacotherapy[1,15]

- Gabapentin to start with 100–300 mg, maximum up to 1800–3600 mg/day
- Pregabalin 50 mg TID or 75 mg BID, maximum up to 300–600 mg/day
- Topical lidocaine 5% up to 3 patches per day.
- Tramadol 50 mg 6 hourly to start with, maximum up to 400 mg per day
- Tricyclic antidepressants such as nortryptyline, desipramine, amitryptiline 10–25 mg HS, maximum dose up to 150 mg
- Morphine 5 mg 6 hourly, to be titrated at weekly intervals balancing analgesia and side effects.

Invasive Treatments for PHN[16,17]

- *Sympathetic nerve blocks—a second- or third*: Line treatment option in cases where more conservative treatments have been exhausted.
- *Neuraxial blocks*—epidural injections of local anesthetic and steroids.
- *Peripheral nerve blocks*—intercostal nerve blocks.
- *Spinal cord stimulation.*

Others[1]

- Psychological interventions
- Transcutaneous electrical nerve stimulation (TENS).

PREVENTION OF PHN[1,7,8,18,19]

- Vaccines
- Antiviral medication
- Amitriptyline initiated within 48 hours of rash onset in herpes zoster patients
- Gabapentin and pregabalin, along with antiviral therapy.

Conclusions

1. Primary varicella vaccine in children is recommended to prevent chickenpox.
2. Herpes zoster vaccination is recommended for older immunocompromise adults to decrease the incidence of herpes zoster and PHN and to reduce the overall burden of illness.
3. Patients with herpes zoster should be treated with antiviral therapy as rapidly as possible to hasten the rate of healing, minimize neural damage, decrease the pain caused by the acute infection, and decrease the incidence and duration of PHN.
4. Opioid analgesics, tricyclic antidepressants, gabapentin, and pregabalin can be used in patients with herpes zoster to treat acute pain, although it is important to recognize that few studies have investigated the efficacy of such treatments.
5. Tricyclic antidepressants, gabapentin, pregabalin, topical lidocaine patches, opioid analgesics, and tramadol should be used for the treatment of PHN given their well-established efficacy in this and other chronic neuropathic pain conditions.
6. Referral to a pain specialist should be made if pain control is inadequate despite the above measures.

REFERENCES

1. Thakur R, Kent JL, Dworkin RH. Herpes zoster and postherpetic neuralgia. In: Fishman SM, Ballantyne JC, Rathmell JP, editors. Bonica's managent of pain. 4th ed. Philadelphia. Lippincott Williams and Wilkins; 2010.
2. Hurley RW, Henriquez OH, Wu CL. Neuropathic pain syndromes. In: Benzon HT, Rathmell JP, Wu CL, Turk DC, Argoff CE, Hurley RW, editors. Practical management of pain. 5th edition. Philadelphia. Elsevier Inc.; 2014.
3. Kawai K, Yawn BP. Risk factors for herpes zoster: a systematic review and meta-analysis. Mayo Clin Proc. 2017;92:1806–21.
4. Stankus SJ, Dlugopolski M, Packer D. Management of herpes zoster (shingles) and postherpetic neuralgia. Am Fam Physician. 2000 Apr 15;61(8): 2437–44, 2447–8.
5. Patel GA, Siperstein RD, Ragi G, Schwartz RA. Zosteriform lymphangioma circumscriptum. Acta Dermatovenerol Alp Panonica Adriat. 2009 Dec. 18(4):179–82.
6. Herpes. 2007 Sep;14 Suppl 2:35-9 (Author-Volpi A), Gnann JW Jr Varicella-zoster virus: atypical presentations and unusual complications, J Infect Dis, 2002, vol. 186 Suppl 1(pg.91–8).
7. Shingles Vaccination | Herpes Zoster | CDC [Internet]. Cdc.gov. 2018 [cited 1 December 2018]. Available from: https://www.cdc.gov/vaccines/vpd/shingles/index.html
8. [Internet]. Acvip.org. 2018 [cited 1 December 2018]. Available from: https://acvip.org/files/Table%20I-IAP%20Immunization%20 Schedule%202016-Final.pdf
9. Arani RB, Soong Sj, Weiss HL, et al. Phase-specific analysis of herpes zoster associated pain data: a new statistical approach. *Stat Med* 2001:20: 2429–39.
10. Dworkin RH, Gnann jW, Oaklander AL, et al. Diagnosis and assessment of pain associated with herpes zoster and postherpetic neuralgia.] Pain 2008: 9(Suppl 1):537–44.
11. Oaklander AL. The density of remaining nerve endings in human skin with and without postherpetic neuralgia after shingles. Pain 2001:92:139–45.
12. Fields HL, Rowbotham M, Baron R. Postherpetic neuralgia: irritable nociceptors and deafferentation. Neurobiol Dis 1998;5:209–27.
13. Baron R, Saguer M. Postherpetic neuralgia. Are C-nociceptors involved in signaling and maintenance of tactile allodynia? Brain 1993:116: 1477–96.
14. Rowbotham MC, Yosipovitch G, Connolly MK, et al. Cutaneous innervation density in the allodynic form of post herpetic neuralgia. Neurobiol Dis 1996:3(3):205–14.
15. Gilron I, Bailey M, Tu D, et al. Morphine, gabapentin, or their combination for neuropathic pain. N EnglJ Med 2005;352:1324–34.
16. Doi K, Nikai T, Sakura S, et al. Intercostal nerve block with 5% tetracaine for chronic pain syndromes. Clin Anesth 2002; 14:39–41.
17. Harke H, Gretenkort P, Ladleif HU, et al. Spinal cord stimulation in post herpetic neuralgia and in acute herpes zoster pain. Anesth Analg 2002: 94(3):694–700.
18. Bowsher D. The effects of pre-emptive treatment of postherpetic neuralgia with amitryptiline: A randomized, double-blind, placebo-controlled trial. Pain Symptom Manage 1997;13:327–31.
19. Berry JD, Petersen KL. A single dose of gabapentin reduces acute pain and allodynia in patients with herpes zoster. Neurology 2005;65:444–7.

CHAPTER

38

Phantom Limb Pain

Ankit Sodani

INTRODUCTION

Phantom sensation or pain is the continuous perception that a body part exists or is painful, after it has been removed either by trauma or amputation.

There are three elements of the phantom complex:

1. **Phantom sensation** refers to any sensation of the missing limb or organ except pain.
2. **Phantom pain** refers to painful sensations referred to the missing organ or limb.[1]
3. **Stump pain or residual limb pain** refers to pain in the residual part.[2]

There is considerable overlap between these entities and same individual can have all three elements. Phantom sensations or pain occur most commonly in the extremities but may be present in any part of the body.

Epidemiology

Phantom Limb Sensation

- Phantom sensations are more frequent than phantom pain and are experienced by nearly all amputees (85–98%) in the first 3 weeks after amputation.[3]
- Immediately after amputation, the phantom limb often resembles the pre amputation limb in shape, length, and volume.
- They usually do not pose a major clinical problem; however in some amputees it may be moderately to severely troublesome.
- Generally resolve after 2 to 3 years without treatment.

Phantom Limb Pain[4]

- Can occur in up to 88% of amputees.
- Can occur as early as 1 week and as late as 40 years after amputation.
- It is less frequent in very young children and congenital amputees.
- It is primarily localized to the distal parts of the missing limb.
- In upper limb amputees, pain is normally felt in the fingers and palm of the hand.
- In lower limb amputees, it is generally experienced in the toes, foot, or ankle.
- The severity and intensity of phantom pain attacks generally decrease with time.

Stump Pain

- It has prevalence of up to 50% of amputees.[2]
- It usually coincides with the development of phantom limb pain.

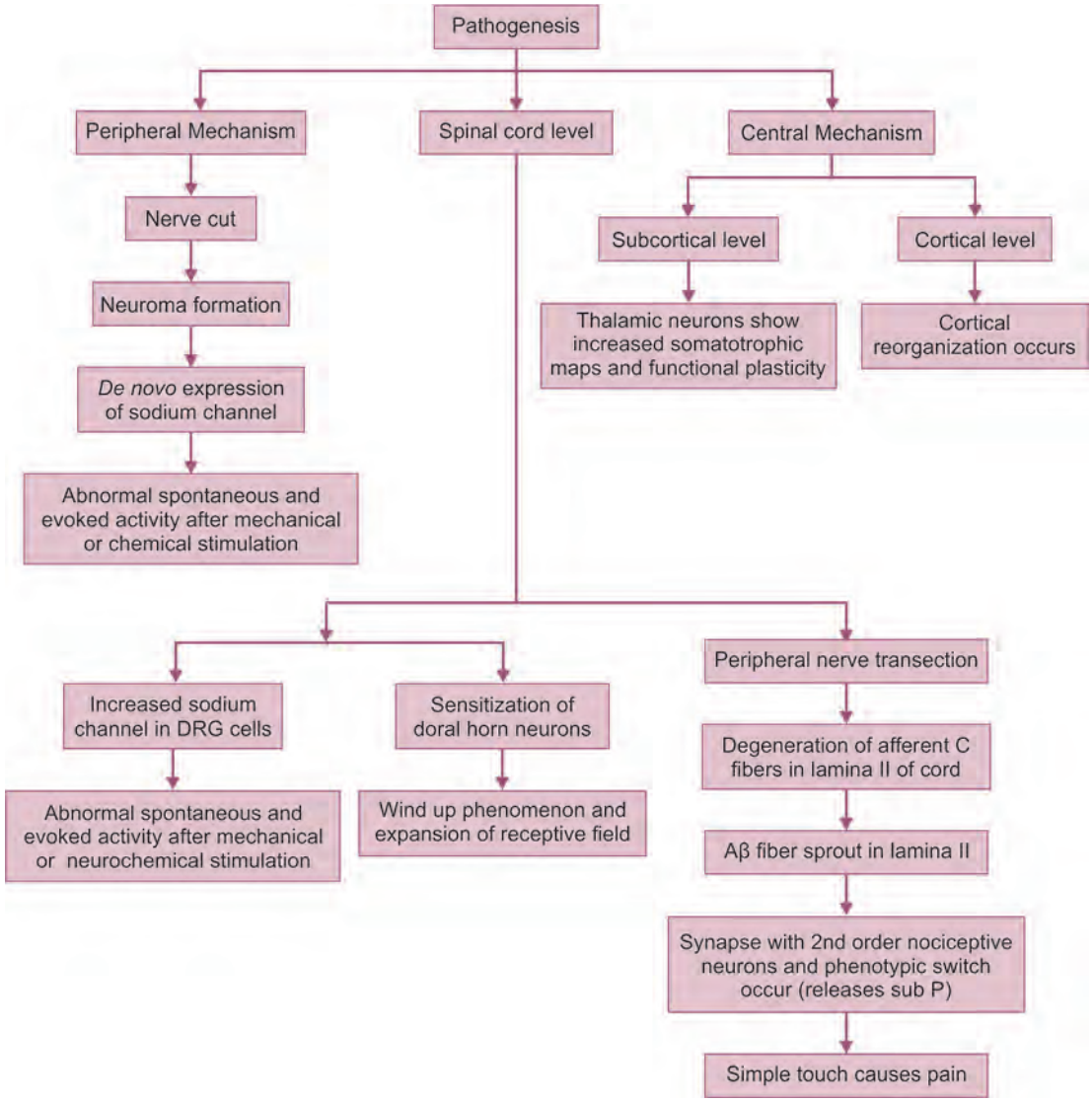
Risk Factors

Risk factor include female sex, upper extremity amputation, presence of preamputation pain, residual pain in remaining limb and time after amputation.

Etiology and Pathogenesis

The etiology and pathophysiologic mechanisms of phantom pain are not clearly understood. Peripheral and central neuronal mechanisms and psychological mechanisms are likely.[5–8]

Neuromatrix and neurosignature theory prorposed by Ronald Melzalk in 1989 states


Pathogenesis
Peripheral Mechanism
Spinal cord level
Central Mechanism
Nerve cut
Neuroma formation
De novo expression of sodium channel
Abnormal spontaneous and evoked activity after mechanical or chemical stimulation
Subcortical level
Cortical level
Thalamic neurons show increased somatotrophic maps and functional plasticity
Cortical reorganization occurs
Increased sodium channel in DRG cells
Sensitization of doral horn neurons
Abnormal spontaneous and evoked activity after mechanical or neurochemical stimulation
Wind up phenomenon and expansion of receptive field
Peripheral nerve transection
Degeneration of afferent C fibers in lamina II of cord
Aβ fiber sprout in lamina II
Synapse with 2nd order nociceptive neurons and phenotypic switch occur (releases sub P)
Simple touch causes pain

that neuromatrix can be coceptualized as a network of neurons within the brain that integrates numerous inputs from areas which then results in output pattern that evokes pain or other meaningful experiences. Neurosignature refers to pattern of activity generated within the brain that are continously being updated based upon one's conscious awareness and perception of body and self. Deprivation of various inputs from the limbs to the neuromatrix causes an abnormal neurosignature to be produced that results in generation of phantom limb pain.

Stump Pain

- Associated with definite pathologic findings skin disease, circulatory disturbances, infection of the skin or underlying tissue, bone spurs, or neuromas.

However, stump pain and phantom pain may occur without obvious stump disorders.

Symptoms and Signs

Phantom Sensation

- Phantom sensations are generally described as normal or as pleasant warmth and tingling.
- The strongest sensations come from body parts with the highest brain cortical representation, such as fingers and toes.
- The phantom limb may undergo "telescoping,"[2] in which the patient loses sensations from the midportion of the limb, with subsequent shortening of the phantom.
- During telescoping, the last body parts to disappear are those with the highest representation in the cortex, such as the thumb, index finger, and big toe.
- Telescoping occurs only with painless phantoms, and it is most common in the upper extremity. Lengthening of the phantom may occur if pain returns.

Phantom Pain

- Primarily localized in distal parts of the missing limb.
- It is usually intermittent but few patients are in constant pain.
- The pain is usually described as burning, aching, or cramping.
- However, it can be crushing, twisting, grinding, tingling, drawing, stabbing with needles, knifelike, sticking, burning, squeezing, sharp, shock like, excruciating.
- Phantom pain may mimic preamputation pain—not only in location, but also in character.

Stump Pain

- Located in the stump itself
- Frequently described as pressing, throbbing, burning, or squeezing.

Super-added Sensations

These are the sensation of an object such as wristwatch, or shoe still being present on the phantom.

Sunderland[9], divided patients into four groups based on their frequency and severity of pain and the degree to which pain interferes with their lifestyle.

Group I—Mild, intermittent paresthesias, not interfering with normal activity, work, or sleep.

Group II—Uncomfortable and annoying paresthesias but do not interfere with activities or sleep.

Group III—Bearable intensity pain, that intermittently interferes with lifestyle, and may respond to conservative treatment.

Group IV—Nearly constant and severe pain that interferes with normal activity and sleep.

Physical Examination

- Physical examination is not very useful except for the trigger points in the stump.
- Physical examination may reveal altered sensitivity in the stump and 20% patients can have neuromas.
- The stump may be cold, and thermography may be a useful diagnostic test if symptoms consistent with reflex sympathetic dystrophy are present.
- Painful scar and bony spur can be present in case of stump pain.
- Contracture of joint proximal to stump can give stump pain.

Diagnostic Testing

Except for the physical abnormalities noted on physical examination, no proven diagnostic test exists for evaluating phantom pain or stump pain.

Differential Diagnosis

Generally natural history of phantom limb pain is to remain unchanged or to improve gradually. Thus, if symptoms increase in severity or if they start after long periods of time after amputation, a differential diagnosis must be entertained.

- Radicular pain[10]
- New-onset herpes zoster or reactivation of

herpes zoster[11]

- Angina may manifest as exacerbated phantom limb pain of upper limb.[12]
- In patients undergoing amputation secondary to malignant disease, if phantom limb pain increases significantly, metastatic disease should be evaluated.[13]

Phantom Limb Pain Treatment[14,15]

Treatment of phantom limb pain or stump pain continues to be difficult and has not been very successful. No data till date has shown to be an effective treatment modality. **Multimodal approach has better success rate and is the preferred modality of treatment**. Initial treatment should be low-risk, low-cost, and noninvasive with more expensive and invasive treatments reserved for patients in whom conservative treatment fails. Treatment options are:

A. Medical management
B. Adjuvant therapy
C. Interventional management.

Medical Management

It is the most common and widely used treatment modality. Anticonvulsants and antidepressants are most commonly used class of drugs with better success rates.

- **Antidepressants:** TCA's like amitryptiline and sodium channel blockers have shown beneficial effects.
- **Anticonvulsants:** Gabapentine is the most commonly used drug. Sedation is seen with this drug but with time patients become tolerant to this side effect. It can be used safely for long-term. Carbamazepine is also an other option.
- **Membrane stabilizers:** IV lignocaine and oral antiarrhythmic agent mexiletene have been found to be effective in neuropathic pain.
- **Opioids:** The role of opioids in neuropathic pain is controversial.
- **NMDA antagonists:** Ketamine and other NMDA receptor antagonist have been found to reduce pain, hyperalgesia and wind up phenomenon.
- **Topical capsaicin:** Extract of hot chilli pepper, agonist for vanilloid receptor (TRPV1) which is present on afferent nociceptor terminals.

Adjuvant Therapy

- **Physical therapy:** It has shown promising results, especially, the educational aspect with attention to stump and preparation for prosthesis. Phantom limb pain is most commonly seen in patients who are unable to use prosthesis within the first 6 months following amputation.
- **Acupuncture, TENS, electroconvulsive therapy:** It have been studied in numerous studies with variable results.
- **Psychological therapy:** Biofeedback and hypnosis can be tried.
- **Mirror therapy:** Proposed by Ramachandran and Rogers in 1996. Patients with amputated limb use either a mirror or mirror box to reflect an image of the intact limb. It is based on the theory that brain has become accustomed to the fact that phantom limb is paralyzed because there is no feedback from the phantom back to brain. Mirror therapy gives brain positive feedback to the mirror neurons[16] that the phantom

Fig. 38.1: Mirror box therapy for phantom limb pain

has moved, i.e. phantom limb becomes unparalyzed (Fig. 38.1).

Interventions

Can be tried when patient is not responding to the medical management. Some of these treatments have more complications than success. Available options are:

- **Stump revision:** If obvious stump pathology is present.
- **Sympathectomy:** Trigger point injections, peripheral nerve block, epidural or subarachnoid blocks.
- **Spinal cord posterior column:** Stimulation is the most common neurosurgical technique used for treatment of phantom limb pain.
- **Neuroablative:** Procedures include stereotactic thermocoagulation lesion in dorsal lateral midbrain, dorsal root entry zone (DREZ) lesioning, lobectomy, corpectomy. Rhizotomy.

Prevention

Knowledge about the mechanisms involved in the development and perpetuation of neuropathic pain should allow a more rational approach to its prevention. Earlier pre- and postsurgical epidural blockade was thought to reduce the incidence of phantom limb pain but various studies have questioned this and hence utility of this approach is still controversial. Advances in neuroimaging techniques are unveiling some keys to the problem. The current emphasis is on the changes taking place in the central nervous system following deafferentation. It seems that the ability to prevent phantom limb or stump pain depends on a capability to modulate the plasticity of the central nervous system. Studies have shown that the problem needs a broad-based approach, including control of perioperative pain and inflammation, adequate counseling and follow-up of the patients, correct surgical technique and long-term rehabilitation, and the use of pharmacologic and behavioral approaches.

Multiple investigators have tried combining psychological preparation, drug therapy, epidural anesthesia, and regional nerve blocks to reduce the occurrence of phantom limb pain and to delay or stop the process of progression from acute to chronic pain. It has been shown that phantom limb pain may be prevented by appropriate psychological counseling of the patients preoperatively.

Conclusion

Phantom pain remains an incompletely understood, difficult to treat chronic painful condition. It is present in a majority of patients following amputation. Phantom pain appears to be caused by the involvement of supraspinal mechanisms. It is thought to be caused by cortical restructuring in the brain. Optimal treatment approach involves the involvement of an interdisciplinary pain medicine team familiar with the therapy of postamputation pain syndromes to achieve a better outcome.

REFERENCES

1. Nikolajsen L, Ilkjaer S, Kroner K, et al. The influence of preamputation pain on postamputation stump and phantom pain. 1997;72:393–405.
2. Jensen TS, Krebs B, Nielsen J, et al. Phantom limb, phantom pain and stump pain in amputees during the first 6 months following limb amputation. 1983;17:243–56.
3. Smith DG, Ehde DM, Legro MW, et al. Phantom limb, residual limb and back pain after lower extermity amputation. 1999;361:29–38.
4. Jensen TS, Krebs B, Nielsen j, et al. Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to preamputation limb pain. Sl: Pain, 1985;21:267–78.
5. Flor H. Phantom-limb pain: characteristics, causes, and treatment. Sl. : Lancet, 2002;1:182–9.

6. Black JA, Nikolajsen L, Kroner K, et al. Multiple sodium channel isoforms and mitogen activated protien kinases are present in painful human neuroms. 2008;64:644–53.
7. Nikolajsen L, Ilkjaer S, Jensen TS. Relationship between mechanical sensitivity and postamputation Pain: a prospective study. 2000;4:327–34.
8. Oderre TJ, Katz J. Peripheral and central hyper-excitability: differential signs and symptoms in persistent pain. 1997;20:404–19.
9. Sunderland S. Nerves and nerve injuries. New York: Churchill Livingstone, 1978.
10. Finneson E, Haft H, Krueger EG. Phantom limb syndrome associated with herniated nucleus pulposus. 1957;14:344.
11. Wilson PR, Person JR, Su DW, et al. Herpes zoster reactivation of phantom limb pain. 1978;53:336.
12. Cohen H. Anginal pain in a phantom limb. 1976;2: 475.
13. Sugarbaker PH, Weiss CM, Davidson DD, et al. Increasing phantom limb pain as a symptom of cancer recurrence. 1984;54:373.
14. Waldman S. Pain Managment. 2. 2011:292–9.
15. Fishman SM, Ballantyne JC, Rathmell JP. Bonica's management of pain. 4:331–6.
16. Rossi S, Tecchio F, Pasqualetti P, Ulivelli M, Pizzella V, Romani GL, et al. Somatosensory processing during movement observation in humans. Clin Neurophysiol. 2002; 113:16–24.

CHAPTER

39

Trigeminal Neuralgia

Praneet Singh

Trigeminal neuralgia or *Tic Douloureux* is a unilateral painful disorder that is characterized by brief electric shock like pains, abrupt in onset and termination and is limited to the distribution of one or more divisions of trigeminal nerve.

EPIDEMIOLOGY

Trigeminal neuralgia is the most common form of facial pain in people older than 50 years of age.[1] Annual incidence varies from 4–5 new patients per 100,000 persons. Highest incidence is found in ages between 50 and 70 years with a female preponderance with a ratio of 2:1.[2]

ANATOMICAL CONSIDERATION

The trigeminal ganglion is situated in an impression above the apex of petrous part of temporal bone on the floor of middle cranial fossa, just outside the posterior part of lateral wall of cavernous sinus. The ganglion is located

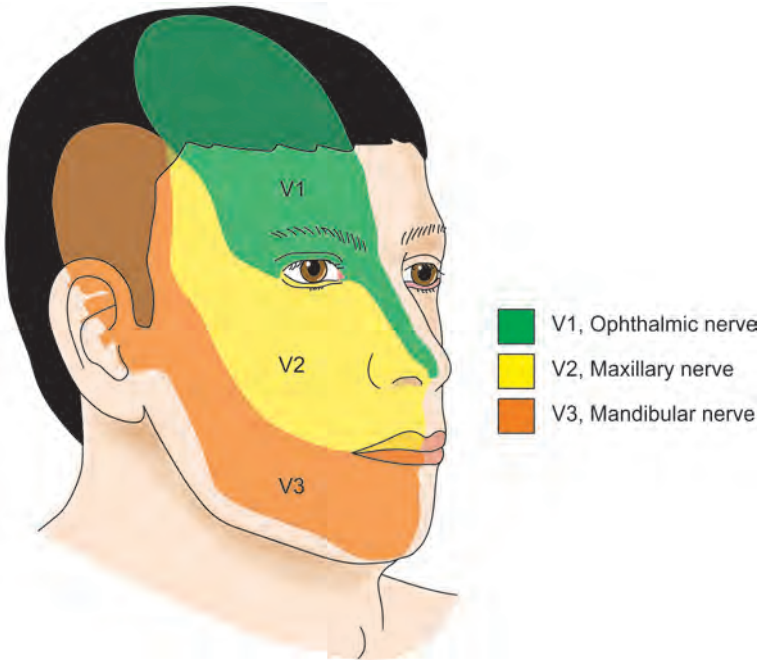


Fig. 39.1

in a dural pouch known as cavum trigeminale (Meckel's cave) which extends forward as a ballooning of the meningeal layer of duramater below the lateral margin of tentorium cerebelli.

Relations of ganglion:

- **Medial:** Cavernous sinus
- **Superior:** Temporal lobe
- **Posterior:** Brainstem
- **Anterior:** Three branches—ophthalmic, maxillary and mandibular nerves.

The origins of these nerves in the ganglion are somatotropically located in the ganglion; the ophthalmic branch is situated most medioposteriorly, the maxillary branch intermediately, and the mandibular branch occupies the ventrolateral position

Ganglion receives communication from the sympathetic plexus around internal carotid artery and gives meningeal twigs to the tentorium cerebelli and floor of middle cranial fossa. Ophthamic division exits the cranial cavity via superior orbital fissure, maxillary division through the foramen rotundum and the mandibular division through foramen ovale (Table 39.1).

Table 39.1. Pain distribution in various nerve branches in trigeminal neuralgia:[2]

V1 only	4 %
V2 only	17%
V3 only	15%
V2 + V3	32%
V1 + V2	14%
V1 + V2 + V3	17%

ETIOLOGY

Trigeminal neuralgia is classified as type 1 and type 2.

1. **Type 1:** Occurs without any apparent cause (other than microvascular compression). It can be purely paroxysmal where patient is pain free between attacks or with concomitant persistent facial pain (trigeminal neuropathy) where a low grade background facial pain persists between attacks. Central sensitization may account for persistent pain.
2. **Type 2:** Trigeminal neuralgia caused by another recognizable disorder that leads to neural damage, e.g. multiple sclerosis, herpes zoster, trauma, space occupying lesion.

PATHOPHYSIOLOGY

The exact pathophysiology is not clear. Clinical observations indicate blood vessels or tumor may cause compression of the trigeminal nerve near the origin of the brainstem, the so-called root entry zone, leading to trigeminal neuralgia. Local pressure results in demyelination leading to abnormal depolarization and ectopic impulses.

DIAGNOSIS

Clinical Presentation (Table 39.2)

Table 39.2. Trigeminal neuralgia: Clinical diagnostic criteria

Site	Within the area of trigeminal nerve sensory distribution
Periodicity	Periods of weeks to months without pain
Duration	Each pain attack lasts seconds but a number of different attacks can occur simultaneously after which there is a pain free interval
Characteristic	Shooting, like an electric shock, stabbing, superficial
Seriousness	Moderate to very intense
Trigger factors	Light touching, such as when eating, talking or washing
Alleviating factors	Frequent sleep, antiepileptics
Accompanying characteristics	Trigger zones, weight loss, poor quality of life, depression

Physical Examination

In patients with idiopathic trigeminal neuralgia, neurological examination is invariably normal, however all cranial nerves needs to be tested. Patients with neurological disorders have secondary trigeminal neuralgia whereby the trigeminal neuralgia is a symptom of another disease, e.g. tumor of the cerebellopontine angle or multiple sclerosis.

Diagnostic Criteria

Diagnosis of trigeminal neuralgia is based on typical clinical features; however the patient needs to undergo an magnetic resonance imaging (MRI) scan to exclude specific pathologies such as a tumor or multiple sclerosis, which could cause a secondary trigeminal neuralgia. The MRI scan is also helpful in cases with a suspected compression of the trigeminal nerve in the posterior cranial fossa.

DIFFERENTIAL DIAGNOSIS[3]

1. **Cranial neuralgias:** Glossopharyngeal neuralgia: Paroxysmal attacks associated with swallowing, chewing, coughing and talking in areas of ear, tonsil, larynx and tongue.

   Geniculate ganglion or nervus intermedius neuralgia: a rare disorder affecting sensory branch of seventh nerve with pain localized in-depth of ear canal.

2. **Trigeminal autonomic cephalgia:** Includes cluster headache, chronic paroxysmal hemicranias, short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT).

3. **Painful ophthalmoplegia:** Tolosa Hunt syndrome, ocular diabetic neuropathy, ophthalmic herpes zoster, ophthalmoplegic migraine.

TREATMENT

Pharmacological (Table 39.3)

The medication of choice is carbamazepine which can reduce pain symptoms in about 70% of cases. Oxcarbazepine has shown similar efficacy with relatively lesser side effects.[4]

Interventional Treatment (Table 39.4)

If the medical treatment is either unsuccessful or has many side effects, an invasive treatment can be carried out.[5] Currently clinically appropriate possibilities are:

1. **Surgical microvascular decompression:** During MVD, the vessels that are in contact with the root entry zone are coagulated and arteries are separated from the nerve using an inert sponge. First choice of treatment in younger patients is MVD.[5]
2. **Stereotactic radiation therapy, gamma knife:** Involves high dose irradiation of a small section of the trigeminal nerve resulting in nonselective damage to gasserian ganglion.
3. **Percutaneous balloon microcompression:** A small balloon (Fogarty's catheter)

Table 39.3: Medical treatments for trigeminal neuralgia

Medication	*Dosage*	*Time to pain relief*	*Side effects*
Carbamazepine	400–800 mg/day	24–48 hours	Rash, aplastic anemia, deranged LFT
Gabapentin	900–2400 mg/day	1 week	Dizziness, somnolence, peripheral edema
Phenytoin	300–500 mg/day	24–48 hours	Rash, hypersensitivity reaction, nystagmus, ataxia
Baclofen	40–80 mg/day	?	Gastric upset, photosensitivity reaction
Lamotrigine	150–400 mg/day	?	Rash, hypersensitivity reaction, CNS and visual symptoms

Table 39.4: comparison of interventional techniques for trigeminal neuralgia

	RF rhizotomy	*Balloon compression*	*Glycerol injection*
Effectiveness	Good	Good	Moderate
Relapse rate	Low	Moderate	High
Success rate	97–100%	99%	85–94%
Facial numbness	98%	72%	60%
Anesthesia dolorosa	1.5%	1.8%	0.1%
Corneal anesthesia	7%	1.5%	3.7%
Motor deficit	24%	66%	1.7%
Ability to target one branch	+	–	–

introduced percutaneosly into the Mekel's cavity compresses the ganglion resulting in ischemic damage. The technique is specially indicated in trigeminal neuralgia involving the V1 division.[6]

4. **Percutaneous glycerol rhizolysis:** Under fluoroscopic guidance, anhydrous glycerol is injected into Meckel's cavity.
5. **Percutaneous radiofrequency treatment:** Considered in elderly patients presenting with trigeminal neuralgia.[7]

REFERENCES

1. Tolle T, Dukes E, Sadosky A. Patient burden of trigeminal neuralgia: results from a cross-sectional survey of health state impairment and treatment patterns in six European countries. Pain Pract. 2006;6:153–60.
2. Rozen TD. Trigeminal neuralgia and glossopharyngeal neuralgia. Neurol Clin. 2004;22:185–206.
3. Nurmikko T. Trigeminal neuralgia. Int J Pain Med Pall Care. 2003;3:2–11.
4. Gronseth G, Cruccu G, Alksne J, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. Neurology. 2008;71: 1183–90.
5. Janetta P. Trigeminal neuralgia: treatment by microvascular decompression. In: Wilkins R, Regachary S, eds. Neurosurgery. New York: McGrawy-Hill; 1996:3961–8.
6. Belber CJ, Rak RA. Balloon compression rhizolysis in the surgical management of trigeminal neuralgia. Neurosurgery. 1987;20:908–13.
7. Mullan S, Lichtor T. Percutaneous microcompression of the trigeminal ganglion for trigeminal neuralgia. J Neurosurg. 1983;59:1007–12.

CHAPTER

40

Myths in Neuropathic Pain

Praneet Singh

Myth: Neuropathic pain can easily be diagnosed with electrophysiological studies (NCS and EMG)

Fact: Electrophysiologic studies consist of electromyography (EMG) and nerve conduction studies (NCS) and have considerable diagnostic value. These studies provide objective evidence of nerve dysfunction that may be too subtle to be found on neurological examination. They can identify sensory and/or motor nerve involvement, differentiate axonal versus demyelinating processes, assess the degree of axonal loss and demyelination, identify chronic versus acute nerve dysfunction, as well as provide localizing information. But it is to be emphasized that electrodiagnostic studies can only measure the large nerve fibers. It is therefore important to understand that neuropathic painful conditions (like: diabetic peripheral neuropathy, CRPS, fibromyalgia, postherpetic neuralgia, etc.) which are mostly because of small fiber abnormality cannot be diagnosed with EMG/NCS.[1]

Myth: Antidepressants in chronic pain states act by treating patient's concurrent depression states

Fact: While concurrent depressive disorders can exist in patients suffering from chronic pain, tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors possess analgesic properties separate from their antidepressant effects. These agents can be useful even in the absence of a coexisting mood disorder. Tricyclic antidepressants including amitriptyline, nortriptyline are effective adjuncts in the treatment of neuropathic pain when used at doses lower than those required to treat depression. The primary mechanism of action of the tricyclic antidepressants is via inhibition of the reuptake of both serotonin and norepinephrine and activating descending inhibitory pathway.[2]

Myth: Prescribing analgesics like morphine, diclofenac, etc. can relieve neuropathic pain

Fact: Nociceptive pain is caused by activation of nociceptive afferent fibers typically through thermal, mechanical, or chemical stimulation. Analgesics drugs including NSAIDs, paracetamol and opioids are used for managing nociceptive pain. Neuropathic pain is caused by damage or dysfunction of any part of the somatosensory system. For managing neuropathic pains, adjuvants or co-anlgesics are required which include antidepressants, anticonvulsants, NMDA receptor antagonists, etc. These drugs are not specifically designed to relieve pain but can help improve pain in neuropathic pain disorders either alone or in combination with other drugs.[3]

Myth: Nerve ablation can relieve neuropathic/nerve injury pain

Fact: Peripheral nerve ablation, though hypothetically seems to be a prudent option for managing peripheral neuropathic pain, however is limited by the complication of deafferentation pains wherein patient develops hyperesthesia and intense burning pain with occasional sharp, shooting pain which may be even more intense than the patient's original pain complaint. Cross talk and ectopic signal generations are a few of the proposed mechanisms. Deafferentation pain has been observed with alcohol/phenol as well as radiofrequency and surgical ablation of nerves.

Myth: Interventional pain management or surgical intervention is must to manage chronic neuropathic pain

Fact: Interventional pain management techniques or surgical interventions including spinal cord stimulators, neuromodulation, etc. form a component of a pain physician's armamentarium for the management of refractory chronic pains. However, certain neuropathic pain states like CRPS, PHN, pharmacotherapy still is considered as the main pillar of therapy. The higher cost of these procedures as well as the chances of failure in a few subset of patients still precludes the adoption of these methods as the first step in management of neuropathic pain states.

REFERENCES

1. Singleton JR, Smith AG, Bromberg MB. Painful sensory polyneuropathy associated with impaired glucose tolerance. Muscle Nerve. 2001 Sep;24(9): 1225–8.
2. Matsuzawa-Yanagida K, Narita M, Nakajima M, Kuzumaki N, Niikura K, Nozaki H, Takagi T, Tamai E, Hareyama N, Terada M, Yamazaki M. Usefulness of antidepressants for improving the neuropathic pain-like state and pain-induced anxiety through actions at different brain sites. Neuropsychopharmacology. 2008 Jul;33(8):1952.
3. Gilron I, Watson CP, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. CMAJ. 2006 Aug 1;175(3):265–75.

SECTION

IX

Interventional Pain Management

Gautum Dass

41. Introduction to Interventional Pain Management
42. Radiofrequency Procedure
43. Cryoneurolysis
44. Ozone in Pain Management
45. Platelet Rich Plasma

CHAPTER 41

Introduction to Interventional Pain Management

Gautam Das

INTRODUCTION

Once the diagnosis is made, pain can be managed in different ways. Traditionally these options are pharmacological, nonpharmacological and surgical. Non-pharmacological methods are exercises, physical therapy, psychological or talking therapy. On the other hand, pain management is commonly done by pharmacotherapy using analgesics, antidepressants, anticonvulsants, etc. In some situations, pain is also managed by different surgeries like total replacement of knee or hip, laminectomy, discectomy, etc. Interventional pain management is comparatively a new specialty that bridges these different pain management options by nerve blocks/ablations or some minimally invasive techniques.

It is defined as "invasive interventions such as the discipline of medicine devoted to the diagnosis and treatment of pain-related disorders principally with the application of interventional techniques in managing subacute, chronic, persistent, and intractable pain, independently or in conjunction with other modalities of treatment."[1]

Diagnostic Interventions

Interventions are done not just to manage pain but also to diagnose the source of pain or finding the pain generator. When clinicians have doubts about the origin of pain, a local anaesthetic can be injected into that tissue or nerve supplying that tissue. If pain relief is more than 50%, it is significant and if it is more than 70%, it is diagnostic.

Sometimes, the diagnostic intervention is repeated with a different and longer-acting local anaesthetic to avoid false-positive results which is common after a single diagnostic intervention. Dual diagnostic intervention is better but may be inconvenient to the patient.

Diagnostic interventions help to identify the source of pain and help to plan definite treatments. It is beneficial before neuroablative interventions.

Advantages

Interventional pain management has several advantages:

- Opioids or other medications can be reduced or stopped. So, side effects of these drugs are reduced.
- The side effects and complications are much less compared to surgical procedures.
- Most interventional procedures are done under local anaesthesia; thus, there are no complications related to general anaesthesia.
- It is an excellent option when surgery can't be done for comorbidities or, when the patient remains unfit for general anaesthesia.
- Most interventional procedures are done as day care procedures, so lesser duration hospital stay and bed occupancy will be less.
- Interventional procedures are much less expensive compared to surgeries or prolonged medications.

- Interventional procedures are applicable in situations where there were no good options for pain management, including surgeries.

Disadvantages

Interventional pain management is safer than surgical procedures but interventional procedures are also risky. The following are disadvantages of interventional procedures:

- Some interventional procedures like vertebroplasty are very risky.
- Adequate skills are mandatory to perform interventional pain management procedures.
- Proper set-up and equipment are needed; these are not readily available in general hospitals who don not have a pain management department.
- Interventions are less costly than surgeries, but these are initially costlier than pharmacotherapy or non-pharmacological management.

Preparation for Interventional Procedures

- Investigations are done to confirm the diagnosis and rule out differential diagnoses.
- Contraindications like uncontrolled diabetes, bleeding disorders, or infections must be ruled out clinically and with appropriate investigations.
- Patient should be explained about the procedures, their risks, and benefits.
- Patient should be kept nil per mouth for a few hours before the procedure.

Precautions During Procedure

- Secure an intravenous line for managing any unwanted adverse reactions.
- Identify any complications early and manage the complications as early as possible.
- Perform procedures under the supervision of seniors during initial days.

Post-procedure Care

- Observe the patient after the procedure for adequate time before discharge.
- At the time of discharge, explain about danger signals and when to report to pain clinic.
- Provide an emergency contact number.

REFERENCE

1. The National Uniform Claims Committee. Specialty Designation for Interventional Pain Management-09. Retrieved 15 April 2021.

CHAPTER

42

Radiofrequency Ablation

Basavaraj Kanthi

INTRODUCTION

Radiofrequency ablation is an interventional procedure that uses thermal energy to ablate nerves carrying nociceptive signals. The thermal energy is created using high-frequency alternating current. The process is called radiofrequency because the alternating current frequency is similar to the frequency of radio wave transmission.

History

Radiofrequency in pain management was first used in 1965 for percutaneous lateral cordotomy for unilateral pain in cancer patients.[1] It was first performed in spinal pain by Shealy in 1975 for RF lesioning of medial branches for lumbar facet joint pain.[2]

Principle of Radiofrequency Procedures

Radiofrequency generator has input current frequency of 50 Hz but output current frequency is of 300,000 Hz. When this low energy high frequency current is passed inside a live body by needle electrode, the ionic particles inside our body and around the electrode start oscillating at 300000 Hz. It causes friction between oppositely charged particles or neutral particles and thus heat is generated. The electrode is an insulated cannula (14–22 G) with 2-15 mm exposed tip. Through this cannula a 27 G thermocouple probe is passed.[3–5]

RF CIRCUIT

It comprises of:

1. RF generator converts 50 Hz alternating current to 300000 Hz and monitors voltage, current, wattage, and temperature.
2. Insulated thermocouple probe is inserted inside RF cannula. It is the site of heat generation, it senses the temperature and sends feedback to the generator.
3. RF cannula with active tip is the site where the lesion is produced.
4. Ground pad is the dispersive plate with a large surface area.

TYPES

1. Conventional RF
2. Pulsed RF
3. Cooled RF
4. Bipolar RF
5. Multichannel RF

CONVENTIONAL RF

- The flow of alternating current is continuous and the RF generator controls the heat generated by reducing the wattage.
- The lesion generated at the active tip is like a match-stick shape with a 2–4 mm diameter.
- The tip temperature varies from 60–90 degrees, with the time of lesion ranging 60–120 seconds.

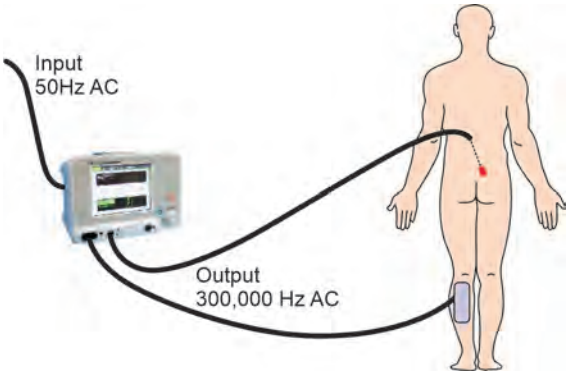


Fig. 42.1

- Conventional RF produces more significant lesion towards its shaft, so the RF cannula should be placed parallel to the nerve.
- The nerve is regenerated in the future, and the average pain-free period varies for the type of nerve. A pain-free period is 3–4 years in a correctly performed lesion.
- Indications-Ablation of Gasserian ganglion[6] lumbar facet, splanchnic, sphenopalatine, lumbar sympathetic.

PULSED RF

- Principle-electromagnetic field produces lesion.
- Two bursts of 20 ms active phase delivered in 1 sec with a silence of 480 ms to maintain a tip temperature of 42 degrees. Time of lesion ranging 6 minutes to 120 minutes.
- Pulsed RF produces bigger diameter lesions towards its tip, so the tip should be perpendicular to the targeting nerve.
- Pulsed RF is done when important structures are there near.
- The nerve is repaired in pulsed RF. Average pain-free period of 4–24 months.
- Indications- Occipital nerve, suprascapular nerve, intercostal nerve, cervical/thoracic/lumbar dorsal root ganglion.

COOLED RF

- Principle- Tip temperature is controlled by circulating water at room temperature. Unlike the conventional RF, the power remains higher, producing a larger, spherical-shaped lesion.
- The needle can be placed at any angle to the targeting nerve.
- Tip temperature varies from 60–80 degrees with a lesion time of 2.30 minutes.
- Cooled RF is a better choice to target larger structures.
- Indications- Genicular nerves of the knee, lateral branches of S1, 2, 3 for SI Joint arthritis, articular branches of shoulder and hip.

BIPOLAR RF

- Current flows between two RF cannulas producing wider size lesion compared to a monopolar probe. It does not require ground pad to complete the circuit.
- Indications-Ganglion Impar, lateral branches of S1, 2, 3 for SI Joint arthritis.

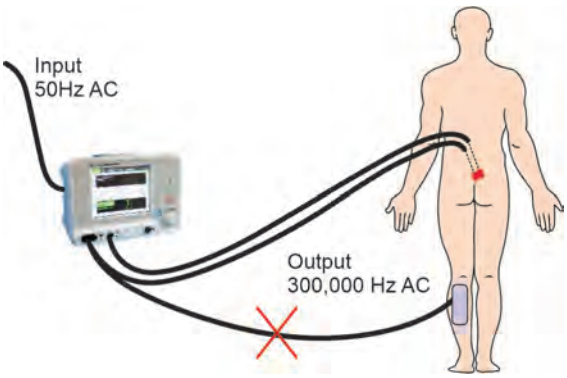


Fig. 42.2

MULTICHANNEL RF

- In multichannel RF we can simultaneously do ablation with more than two probes. Unlike bipolar, here ground pad is needed to complete the circuit.

TIME VS LESION SIZE

Most of the increase in the lesion size occurs within 60 to 90 seconds. After 90 seconds, further growth is prevented due to increasing

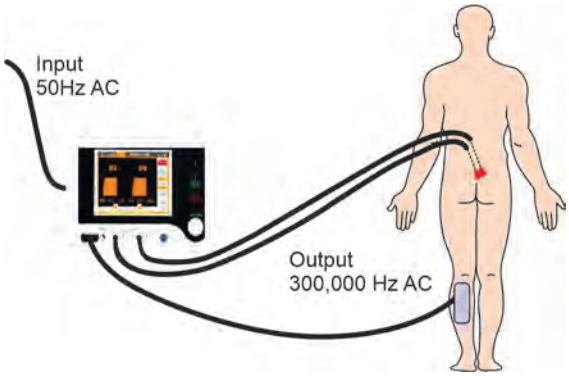


Fig. 42.3

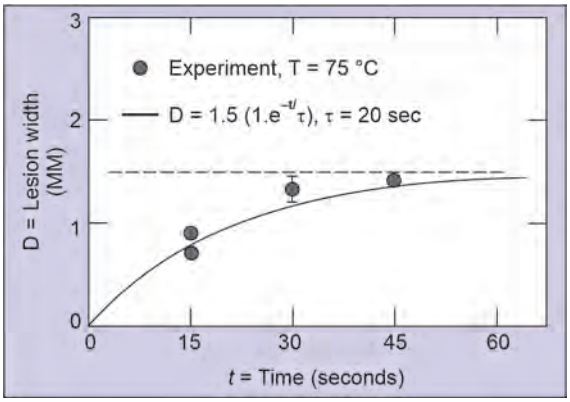


Fig. 42.4

impedance by the coagulated tissues to the flow of current.[7]

CONFIRMATION OF NEEDLE PLACEMENT

- Image guidance (C arm or USG)
- Sensory testing—done at 50 Hz current frequency, amplitude 0.5 V, paraesthesia should be produced in the same area of distribution of pain.
- Motor testing—at 2 Hz with 2V amplitude, undesired muscles should not contract.
- Sensory-motor dissociation: It is done when sensory and motor fibres are close to each other. Needle is placed close to sensory part and away from motor part. Sensory fibres are stimulated at 50 Hz with amplitude as low as possible (0.25 V), then increase the amplitude to more than double (0.5 V)

REFERENCES

1. Rosomoff HL, Carroll F, Brown J, Sheptak P. Percutaneous radiofrequency cervical cordotomy: technique. Journal of neurosurgery. 1965 Dec 1; 23(6): 639–44.
2. Shealy CN. Percutaneous radiofrequency denervation of spinal facets: treatment for chronic back pain and sciatica. Journal of neurosurgery. 1975 Oct 1; 43(4): 448–51.
3. Foster KR. Thermal and nonthermal mechanisms of interaction of radio-frequency energy with biological systems. IEEE Transactions on Plasma Science. 2000 Feb; 28(1): 15–23.
4. Organ LW. Electrophysiologic principles of radiofrequency lesion making. Stereotactic and Functional Neurosurgery. 1976; 39(2): 69–76.
5. Bogduk N, Aprill C, Dreyfuss P. International Spine Intervention Society, Practice Guidelines for Spinal Diagnostic and Treatment Procedures. San Francisco: International Spine Intervention Society. 2013; 409.
6. Kanpolat Y, Savas A, Bekar A, Berk C. Percutaneous controlled radiofrequency trigeminal rhizotomy for the treatment of idiopathic trigeminal neuralgia: 25-year experience with 1600 patients. Neurosurgery. 2001 Mar 1; 48(3): 524–34.
7. Lord SM, McDonald GJ, Bogduk N. Percutaneous radiofrequency neurotomy of the cervical medial branches: a validated treatment for cervical zygapophysial joint pain. Neurosurgery Quarterly. 1998 Dec 1; 8(4): 288–308.

CHAPTER

43

Cryoneurolysis

Sneha Shreyas

INTRODUCTION

Cryoneurolysis refers to applying extreme cold upon pain carrying nerves to abolish pain by creating a second-degree nerve lesion (Axonotmesis). Application of cryoneurolysis method initiates a cascade of pathophysiological events interrupting conduction of painful stimulus with fully reversible 2nd degree nerve damage.

Lloyd, et al. coined the term "cryoanalgesia" for its use in pain management. He proposed that this cryoneurolysis was superior to other methods like chemical neurolysis using alcohol, phenol because it is not followed by neuritis or neuralgia. It is a safe and advanced procedure with minimal risk of complications when performed under image guidance.

History of Application of Cold in Medicine

1899—Campbell White was the first to use refrigerants medically.

1950—Allington was first to use liquid nitrogen for medical treatments.

1961—Cooper created an early cryoprobe that reached –190°C using liquid nitrogen.

1967—Amoils, an ophthalmic surgeon used carbon dioxide and nitrous oxide to create a cryoprobe that reached –70°C

1974—Nelson KM Intraoperative intercostal nerve freezing to prevent post-thoracotomy pain.[1]

1976—Lloyd JW-Cryoanalgesia: a new approach to pain relief was published in Lancet.[2]

Cryo Physics

Cryoprobes consists of hollow tube with smaller inner tube. A compressed gas (CO_2 or Nitrous oxide) at high pressure of 600–800 psi travels through the outer tube and is released into inner tube through a tiny aperture (0.002 mm) at the tip. Gas which is released at 10–15 psi expands and temperature is dropped down. This results in ice ball formation at the tip in the temperature range of –70°C.[3] The same principle is used for cooling in refrigerator or air-conditioner. It is called Joules-Thompson effect. It is explained schematically in Fig. 43.1.

Upon application of cold following degrees of nerve injury is possible:

(Sunderland's classification of nerve injury)[4]

1. First degree injury or Neuropraxia—on application of cold from temperature +10 to –20°C, there is conduction block without any anatomical damage. Duration

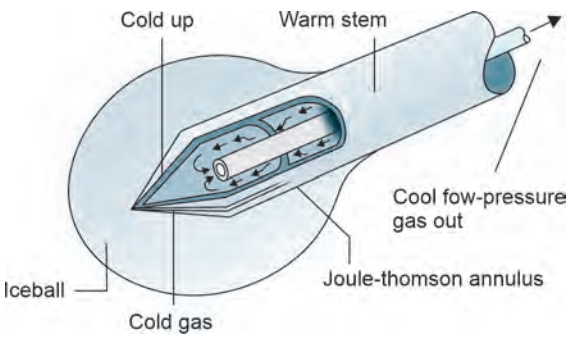


Fig 43.1: Cut section of a cryoprobe to explain Joule-Thomson effect

of analgesia ranges from few hours to maximum of 7 days.

2. Second degree or Axonotmesis—on application of cold from –20°C to –100°C there will be loss of axonal continuity. There will be Wallerian degeneration with preservation of endoneurium, perineurium and epineurium. The nerve will be regenerated fully. Larger diameter fibres like motor fibres, touch fibres will recover within two months whereas pain fibres will take longer time up to two years for full recovery. The recovery will be perfect without any chances of cross-talk or ectopic signals like in 3rd degree nerve damage. This is the goal of cryoneurolysis.
3. Third/fourth degree—on application of temperature beyond –100°C –140°C there will be loss of continuity of endoneurium and perineurium called neurotmesis. The recovery will be further delayed and complete recovery is not possible. Chances of cross-talk and ectopic signal generation are high with development of neuropathic pain.
4. Fifth degree transection (severe neurotmesis)—gross loss of continuity. It is not possible with cryoneurolysis.

Gases used for cryoneurolysis are CO_2 with freezing point of –78°C and N_2O with freezing point of –89°C. So, when we use these gases, temperature is lowered to these levels causing second degree nerve lesion giving best therapeutic pain relief without any possibility of development of neuropathic pain. As the endometrium remains intact, neuroma formation does not occur and nerve will regenerate fully.

The degree of the freezing (and subsequent nerve damage) depends on many factors like:

1. The proximity of the probe to the nerve,
2. The size of the cryoprobe,
3. The size of the ice ball formed at the tip,
4. The rate and duration of freezing,
5. The temperature of the tissues in proximity to the probe.[5]

Cryoprobes

Cryoprobes are blunt and local anaesthetics cannot be injected through it. The cryoprobes vary in size from 12 to 22 G. Lesion size also varies from 6 mm to 15 mm in width and 6 mm to 80 mm in length. In Fig. 43.2 various cryoprobes are shown and ice-balls are shown in Fig. 43.3.

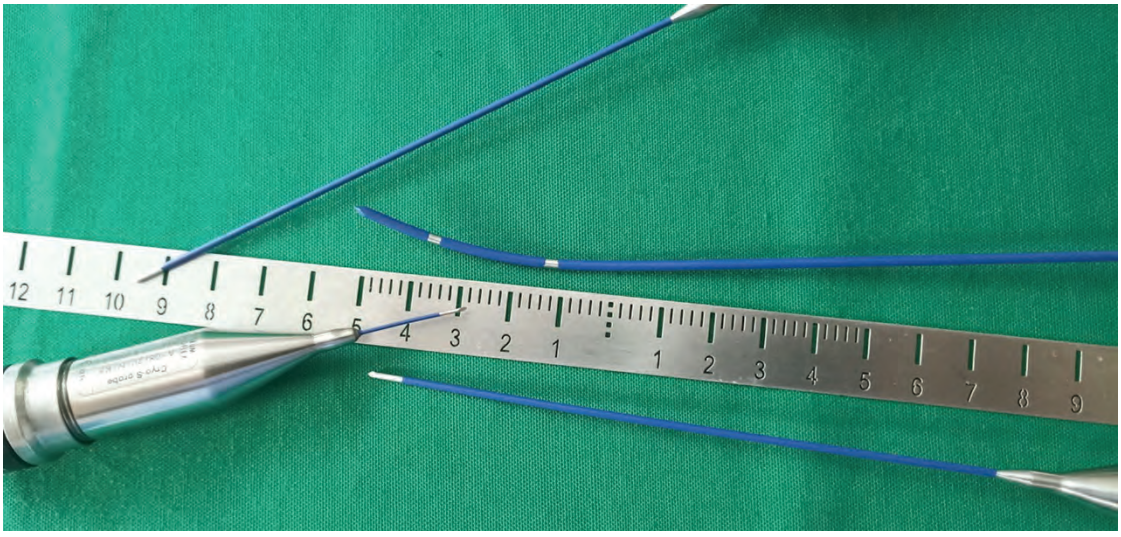


Fig. 43.2: Different cryoprobes

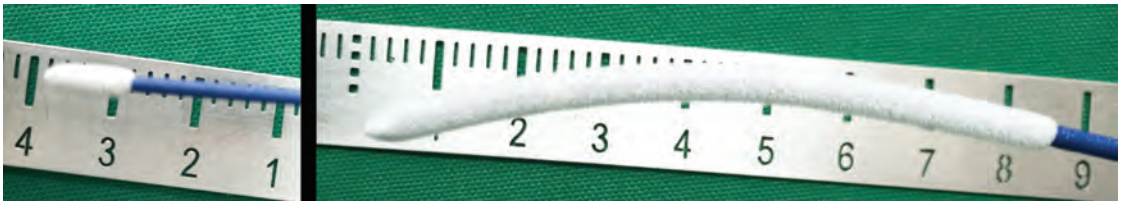


Fig. 43.3: Ice ball at the tip of cryoprobe

Cryo machine comes with a built in neuro-stimulator with two types of stimulation (motor and sensory). Cryoprobes are coated with medical teflon. So stimulation is possible only at the probe tip. All cryoprobes are hyperechogenic under ultrasound. Ice ball formation during cryoneurolysis can be visualised under ultrasound as hyperechoic structure casting an acoustic shadow underneath.

1.3 mm tip cryoprobe will result in lesion up to 15 mm. SI joint probe is curved and has an active tip of 8 cm and results in a long lesion up to 80 mm as shown in Fig. 43.3.

Technique

It requires precise localisation of target nerve under ultrasound or fluoroscopy. Prior confirmation with diagnostic block is necessary before proceeding with cryoneurolysis. Machine and gas supply should be checked and probe is purged of room air gases. After skin infiltration, target structure is confirmed using motor and sensory stimulation.

Gas flows of 10–12 litres per minute are turned up and freeze cycle is initiated. Each freeze cycle is pre programmed for 3 minutes duration which results in optimum density of ice ball. This is followed by defrosting cycle of 60 seconds.

Mechanism of Cryoneurolysis

Ice crystals create vascular damage to the vasa nervorum, which produces severe endoneural oedema. These mechanisms result in vascular injury, which induces a coagulation cascade and eventual ischemia-mediated cellular damage. In the thawing phase of the procedure, water rushes into previously shrunken cells, causing them to burst. This will disrupt the nerve structure and causes wallerian degeneration. But it leaves the myelin sheath and endoneurium intact.

Advantages of Cryoneurolysis

There are several advantages of cryoneurolysis over chemical neurolysis and radio frequency ablation.

- Direct visualization of the ablation zone with use of ultrasound.
- Decreased or no procedural and post-procedural pain, only skin needs to be anaesthetised.
- Cryoneurolysis does not disrupt the epineurium or perineurium. Therefore, it reduces the risk of neuroma formation and allows complete nerve regeneration.
- It avoids the risk of systemic toxicity associated with chemical neurolysis.
- Duration of pain relief upto 2 years.
- Safe and suitable for mixed peripheral nerves.
- Reversible effect, less damage to surrounding tissues.
- Large sized lesion is possible with better results in situations like sacroiliac joint with excellent pain relief.[6]

Contraindications

Cryoneurolysis cannot be done in following situations:

- Infection
- Bleeding disorders
- Cryoglobulinemia
- Cold urticaria
- Raynaud's disease

Indications

Cryoneurolysis has been described in following indications with adequate pain relief:

- Craniofacial pain secondary to trigeminal neuralgia, facial pain syndromes (supra, infra orbital nerve, occipital nerve, mental nerve).
- Medial branch for facet joint pain.
- Supra scapular neuralgia.
- Intercostal neuralgia with multiple conditions including post-thoracotomy neuromas, persistent pain after rib fractures[7] and post herpetic neuralgia in thoracic distribution.
- Abdominal and pelvic pain secondary to ilioinguinal, iliohypogastric, genito femoral, pudendal neuralgia
- Scar neuralgia.
- Sacroiliac joint arthropathy.
- Cluneal nerve.
- Genicular nerves of knee.
- Medial calcaneal nerve for heel pain.
- Phantom limb pain.
- Movement disorders.

Conclusion

Cryoneurolysis is the most advanced technique in pain medicine. It is safe, effective technique and definitely the future of interventional pain management. It provides higher success rate and superior analgesia if used after confirmation of diagnosis with diagnostic

REFERENCES

1. Nelson KM, Vincent RG, Bourke RS, et al. Intraoperative intercostal nerve freezing to prevent postthoracotomy pain. Ann Thorac Surg 1974; 18:280–285.
2. Lloyd JW, Barnard JDW, Glynn CJ. Cryoanalgesia: a new approach to pain relief. Lancet 1976; 2:932–934.
3. Garamy G. Engineering aspects of cryosurgery. In Rand RW, Rinfret A, von Leden H (eds). Cryosurgery, Charles C. Thomas, Springfi eld, 1968.
4. Sunderland S. Nerves and Nerve Injuries. Edinburgh and London: Livingstone, 1968:180.
5. Trescot AM. Cryoanalgesia in interventional pain management. Pain Physician. 2003; 6:345-360, ISSN 1533-3159.
6. Sahoo RK, Das G, Pathak L, Dutta D, Roy C, Bhatia A. Cryoneurolysis of innervation to sacroiliac joints: Technical description and initial results-A case series. A A Pract. 2021;15(4): e0142.
7. Finneran JJ, Gabriel RA, Swisher MW, et al. Ultrasound-guided percutaneous intercostal nerve cryoneurolysis for analgesia following traumatic rib fracture -a case series. *Korean J Anesthesiol*. 2020;73(5):455-459.

CHAPTER

44

Ozone in Pain Management

Syeda Shaista Naz

Ozone is a tri-atomic oxygen molecule (O_3), as compared to Oxygen (O_2). Its name is derived from a Greek word[1] "ozein" meaning "to smell". It has a density of 2.144 grams per litre at STP. Ozone is a dark blue liquid below its boiling point (–112° C) and blue-black crystalline solid below its melting point ("193°C). It is colourless when found in atmosphere. It has a molecular weight of 47.9982 atomic mass unit (amu)[1]. It is the most chemically active form of oxygen.

The ozone molecule is very unstable and has a short half-life of approximately 20 min at 20°C temperature. Therefore, it will decay after some time into its original form, i.e. oxygen as described in the formula below:

$$2O_3 = 3O_2$$

History of Ozone in Medicine

Ozone as a chemical element was discovered at the end of eighteenth century. In 1785, a Dutch physicist by name Martinus Van Marum noted some specific odour by subjecting oxygen to electrical discharges[1]. In 1848, Christian Friedrich Schönbein, a German physicist discovered and named the smelling gas Ozone. Mariniak and Delarive showed that it is an allotropic form of oxygen whereas Mulliken and Dewar clarified its molecular structure.

E. Payer, A. Fish and H. Wolf were the pioneers to apply ozone in medicine in twentieth century. In 1953, Andrews reported on ozone being an allotropic form of oxygen. In 1957, Warner created tubes for magnetic induction, capable to produce ozone in large quantities and that launched an extensive research of ozone properties. Verga has described the use of medical ozone for treatment of low back pain in 1983. In 1998, Muto and Avella suggested an intradiscal injection of ozone for disc herniation under CT guidance[2].

Use of Ozone in Painful Conditions

Ozone has been claimed to be effective in many painful and non-conditions though evidence is not there in every claims. The following painful conditions are treated with ozone with moderate evidences.

- Prolapsed Intervertebral disc with radicular pain (the procedure is called ozone nucleolysis).
- Chronic pain in patients of Osteoarthritis (the procedure is called porlozone therapy).
- Painful sprains of ligaments (the procedure is called prolozone therapy).

Mechanism of Action

The action of ozone is due to the active oxygen atom released by the breakdown of the ozone molecule. Ozone has a dose-related biological action. At high concentrations (30–70 µg/ml O_2), it may cause alterations of tissue structure; at medium concentrations (20–30 µg/ml O_2) it seems to affect the regulation of the immune system and at low concentrations (<20 µg/ml O_2) it improves the microcirculation.[3]

The dose of ozone is crucial and must not exceed the capacity of antioxidant enzyme and glutathione to prevent accumulation of the superoxide anion and hydrogen peroxide, which can cause cell membrane degradation[4].

Viebahn reported that the nontoxic concentration of ozone varies from 1 to 40 µg/ml of oxygen, and concentration of ozone for therapeutic purpose should not exceed 40 µg/ml[5].

Description of an Ozone Generator

When an energetic force such as electricity or ultra-violet light is imposed on an oxygen molecule, the two oxygen atoms are temporarily split into single oxygen atoms. Consequently, oxygen radicals are produced which bonds with oxygen molecule to form Ozone, a gaseous molecule which consists of three oxygen atoms all sharing the same electrons (O_3). Ozone operates on the principle of oxidation. Oxygen (O_2) molecules go into the generator and are exposed to an electric spark. Ozone is produced in a silent electrical discharge within which electrons with sufficient kinetic energy split the O = O bond upon impact resulting in a mixture of oxygen and ozone.

Corona discharge type is the most common generator used for the production of ozone because of the advantages like cost-effectiveness and the greater durability of the system. For the feed inlet, medical grade oxygen is used. When pure oxygen is used, a higher concentration of ozone can be produced.

Ozone Nucleolysis

Ozone Nucleolysis is a minimally invasive procedure done for prolapsed intervertebral disc done by utilising the properties of a gas mixture of oxygen and ozone. It is injected into the prolapsed disc, causing reduction in the size of the disc.

The active oxygen atom or singlet oxygen of ozone is attached to the proteoglycan bridges of the nucleus pulposus. Due to this reaction, proteoglycans are denatured and its osmotic pressure is reduced in the nucleus pulposus and cannot hold water. As a result, there is shrinkage or mummification of the disc leading to decompression of nerve roots. Ozone not only attenuates nerve root compression by reducing the size of the disc, it also helps to reduce venous stasis caused by constriction of vessels and hence improves the microcirculation and supply of oxygen[7]. This reduces pain associated with neuronal hypoxia. In addition, ozone has analgesic and anti-inflammatory effects[8] as it inhibits proinflammatory prostaglandins synthesis, bradykinins release, and allogenic compounds. Ozone also increases the release of antagonists to proinflammatory cytokines[9].

Prolozone Therapy

Prolozone therapy is a technique which combines neural therapy, prolotherapy, and ozone therapy[10]. It involves injecting various combinations of local anaesthetics, anti-inflammatory medications, vitamins, minerals, proliferatives, and a mixture of ozone-oxygen gas into degenerated or injured joints and pain generators resulting in regeneration and reduction of pain.

Chronic pain and trauma in a patient results in decreased oxygen utilization. As oxygen utilization decreases, the ratio of NAD to NADH decreases. A decrease in ratio results in a slowdown of all cellular functions including protein synthesis, cellular division, growth factor function, membrane potential, etc. leading to an increase in free radical damage, which ultimately causes inflammation and oedema. Prolozone helps in re-establishing cellular membrane potentials, anti-inflammation, providing substrates for oxygen utilization which is directly stimulated by ozone. Ozone reacts with the double bonds in lipids and amino acids and creates peroxides that are able to oxidize NADH to NAD, thereby correct the declining NAD/NADH ratio. Thus, cellular function is stimulated and oxygen utilization is returned to normal promoting healing.

Contraindications

- Pregnancy
- Bleeding diathesis
- Coagulation abnormalities
- G6PD deficiency.
- Thrombocytopenia
- Ozone Allergy/Intolerance

Complications

- Intraocular haemorrhage
- Discitis
- Subcutaneous hematoma
- Transient paraesthesia
- Cough, bronchospasm, eye irritation, dryness of mouth and throat as ozone is irritant to the mucus membrane.

REFERENCES

1. Ozone Therapy in Practice. Health Manual. Nizhny Novgorod, Russia, 2008
2. Muto M, Avella F: Percutaneous treatment of herniated lumber disc by intradiscal oxygen-ozone injection. Interventional Neuroradiology 4: 279–286, 1998.
3. Bocci V: Oxygen –ozone Therapy. Acritical evaluation. Kluwer Academic Publishers, Dordrecht, The Netherlands 1–440, 2002.
4. Bellomo C, Mirabelli F, et al. Glutathione-mediated mechanism of defence against free radical-induced hepatotoxicity. Hum Toxicol 8: 152, 1998.
5. Viebahn R: The use of ozone in medicine. Heidelberg Karl F, Haug Publisher; 1994.
6. Debra J. Sponholtz, Michael A. Walters, et al.: A Simple and Efficient Ozone Generator. Journal of Chemical Education/Vol. 76/No. 12 December 1999. JChemEd.chem.wisc.edu
7. G. Das, S. Ray, S. Ishwarari, et al.: Ozone Nucleolysis for Management of Pain and Disability in Prolapsed Lumber Intervertebral Disc—A Prospective Cohort Study. Interventional Neuroradiology 15: 330–334, 2009
8. Iliakis E, Valadakis V, et al.: Rationalization of the activity of medical ozone on intervertebral disc: a histological and biochemical study. Rivista di Neuroradiologia 14 (suppl 1): 23-30, 2001.
9. Bocci V, Luzzi F, et al.: Studies on the biological effects of ozone. III. An attempt to define conditions for optimal induction of cytokines. Lymphokine Cytokine Res 12: 121–126, 1993.
10. Frank Shallenberger: Wonder Why? Prolozone™ Regenerating joints and eliminating pain. Journal of Prolotherapy. 2011;3(2):630–638

CHAPTER

45

Platelet-Rich Plasma

Shalina Chandran

INTRODUCTION

Platelet Rich Plasma (PRP) was introduced in the 1970s to treat thrombocytopenia. The term describes the autologous plasma preparations with enrichment of platelet counts to above that of peripheral blood. In recent times, the use of PRP to enhance tissue regeneration and repair has increased as it is regarded as easy to prepare and inject, well-tolerated, less aggressive than other treatment modalities, and with minimal complications. In pain medicine, it is now widely used to treat osteoarthritis, tendinopathy, acute and chronic soft tissue injuries, and muscle or ligament tear.

Definition

PRP is defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline.[1] PRP's working definition is shifting to having a minimum platelet concentration of 1 000 000/μL or approximately a fivefold increase in platelets from baseline.[2]

Mechanism of Action

Platelets are a rich source of growth factors and cytokines, including platelet-derived growth factor αβ (PDGF-αβ), transforming growth factor β1 (TGF-β1), and vascular endothelial growth factor (VEGF). Activation of platelets leads to the release of these growth factors which play a crucial role in the healing process by directing cell proliferation, chemotaxis, and angiogenesis.[2]

Overview of PRP Preparation

Whole blood collected → anticoagulant added → centrifuged → blood separated into components → PRP obtained (Fig. 45.1).

Fig. 45.1: Centrifuge

Techniques for PRP Preparation

- *Open technique:* Exposure to a working environment with contact to different materials like pipettes or collection tubes and hence high chance of contamination.
- *Closed technique:* Commercial devices with CE marking involving centrifugation are used; thus, environmental exposure is not there (recommended).[1]

On the day of the procedure, it is important to document the individual's platelet count and also the absolute number of platelets/μL in the preparation of PRP. Preparation methods, collected whole blood volume, relative force and time of centrifugation, and

single or double centrifugation spins all affect the concentration and quality of PRP. However, there is no consensus for which method is superior, how many centrifugations are required, or at what speed and duration of spin.[3]

There are mainly two varieties of PRP preparations based on the white blood cell (WBC) count. These are leukocyte-rich PRP preparations where WBC counts are above baseline, and leukocyte poor PRP preparations, where WBC counts are below the baseline.[4]

PRP is prepared by differential centrifugation either by the PRP method or the buffy-coat method. The initial spin seeks to separate red blood cells and platelet-poor plasma from the 'buffy coat', a layer rich in WBCs and platelets. PRP can be derived from the buffy coat or the platelet-poor plasma. There is no consensus yet on whether WBC inclusion in the final injectate is beneficial or merely causes unnecessary inflammation, so additional spins either remove or keep the WBCs with further processing to isolate the platelet concentrate for use.[5]

Numerous commercial PRP kits are now available. These PRP systems claim to yield higher platelet counts than manual laboratory preparations consistently (Fig. 45.2).

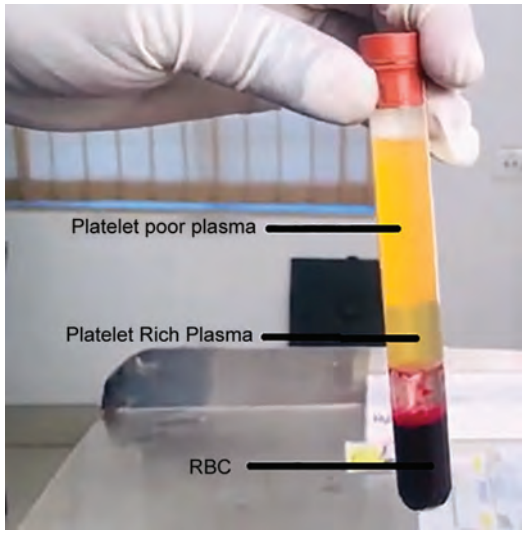


Fig. 45.2: PRP

Contraindications (Table 45.1)

Effectiveness of PRP

PRP does not provide immediate pain relief. It usually takes 3–4 weeks, and after that, pain continues to improve through 3 to 6 months.[2] There is also a wide variation in the recovery period, ranging from 3 months-12 months.

ISSP Coding System for Uniform Nomenclature of Interventional Pain Procedures[8]

PRP of major joint/bursa: MIPSI-I-001
PRP of intermediate joint/bursa: MIPSI-I-002
PRP of minor joint/bursa: MIPSI-I-003

Clinical Pearls

- Strict asepsis to be maintained.
- Acid Citrate Dextrose Solution A (ACD-A) is the anticoagulant used in preparing PRP.

Table 45.1: Contraindications of PRP[7]

Absolute contraindications	*Relative contraindications*
• Platelet dysfunction syndrome	• Consistent use of NSAIDs within 48 hours of procedure
• Critical thrombocytopenia	• Corticosteroid injection at treatment site within 1 month
• Hemodynamic instability	• Systemic use of corticosteroids within 2 weeks
• Septicaemia	• Tobacco use
• Local infection at procedure site	• Recent fever or illness
• Patient unwilling to accept risks	• Cancer-especially hematopoietic or bone
	• Haemoglobin less than 10 g/dl
	• Platelet count less than 105/µl

- We use the closed, single-spin method at 3500 rpm for 15 minutes.
- PRP to be used within 30 minutes of preparation.
- 10 ml whole blood usually yields 1-2 ml of PRP.
- Hyaluronic acid can be added to activate PRP.
- No NSAIDs or steroids after PRP.
- Ice application and paracetamol/tramadol can be used for pain relief.

REFERENCES

1. Pathak L, Das G, Roy C, et al. Platelet-rich Plasma: A Recent Review. J Recent Adv Pain 2020;6(1):20–23.
2. Sharma K, Das G, Sarvesh B, Agarwal A. Platelet-rich plasma for degenerative knee joints: What is the evidence? Indian J Pain 2019;33:126-30
3. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin Appendage Disord 2018;4 (1):18–24. DOI: 10.1159/000477353.
4. Le A.D.K., Enweze L., DeBaun M.R., Dragoo J.L. Current clinical recommendations for use of platelet-rich plasma. Curr. Rev. Musculoskelet Med. 2018;11:624–634. DOI: 10.1007/s12178-018-9527-7.
5. Fadadu PP, Mazzola AJ, Hunter CW, et al. Review of concentration yields in commercially available platelet-rich plasma (PRP) systems: a call for PRP standardization.Regional Anesthesia and Pain Medicine 2019;44:652–659.
6. Ramaswamy Reddy SH, Reddy R, Babu NC, Ashok GN. Stem-cell therapy and platelet-rich plasma in regenerative medicines: A review on pros and cons of the technologies. J Oral Maxillofac Pathol. 2018; 22(3):367-374. doi:10.4103/jomfp.JOMFP_93_18
7. Harmon K, Hanson R, Bowen J, Greenberg S, Magaziner E, Vandenbosch J, et al: Guidelines for the use of platelet rich plasma. https://www.scribd.com/document/159334949/206-ICMS-Guidelines-for-the-Use-of-Platelet-Rich-Plasma-Draftob-oasbonasdandbowndoww.
8. Surange PN. ISSP coding system uniform nomenclature for interventional pain procedures. Indian J Pain 2019;33:51–3

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